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FIG. 1.

FIG. 2

FIG. 3.

PLATE I.

Fig. 1.—Parasite of quartan infection. Fig. 2.—Parasite of benign tertian infection. Fig. 3.—Parasite of malignant tertian infection ("æstivo-autumnal"). *(Compiled from Thayer and Hewetson.)*

A Manual of the Diseases of Warm Climates

BY

PATRICK MANSON, M.D., LL.D.

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TROPICAL DISEASES

A Manual of the Diseases of Warm Climates

BY

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PREFACE.

A MANUAL on the diseases of warm climates, of handy size, and yet giving adequate information, has long been a want; for the exigencies of travel and of tropical life are, as a rule, incompatible with big volumes and large libraries. This is the reason for the present work.

While it is hoped that the book may prove of practical service, it makes no pretension to being anything more than an introduction to the important department of medicine of which it treats; in no sense is it put forward as a complete treatise, or as being in this respect comparable to the more elaborate works by Davidson, Scheube, Rho, Laveran, Corre, Roux, and other systematic writers in the same field.

The author avails himself of this opportunity to acknowledge the valuable assistance he has received, in revising the text, from Dr. L. Westenra Sambon and Mr. David Rees, M.R.C.P., L.R.C.P., lately Senior House Surgeon, Seamen's Hospital, Albert Docks, London. He would also acknowledge his great obligation to Mr. Richard Muir, Pathological Laboratory, Edinburgh University, for his care and skill in preparing the illustrations.

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INTRODUCTION.

THE ÆTIOLOGY OF TROPICAL DISEASES.

THE title which I have elected to give to this work, TROPICAL DISEASES, is more convenient than accurate. If by "tropical diseases" be meant diseases peculiar to, and confined to, the tropics, then half a dozen pages might have sufficed for their description; for, at most, only two or three comparatively unimportant diseases strictly deserve that title. If, on the other hand, the expression "tropical diseases" be held to include all diseases occurring in the tropics, then the work would require to cover almost the entire range of medicine; for the diseases of temperate climates are also, and in almost every instance, to be found in tropical climates.

I employ the term "tropical" in a meteorological rather than in a geographical sense, meaning by it sustained high atmospheric temperature; and by the term "tropical diseases," I wish to indicate diseases occurring only, or which from one circumstance or another are specially prevalent, in warm climates.

It must not be inferred from this, however, that high atmospheric temperature is the sole and direct cause of the bulk of tropical diseases. The physiological machinery of the human body is so adjusted that great variations of atmospheric temperature can be supported by man with impunity. Indeed, although temperature acts as an important pathogenic factor, it is very rarely that it does so directly. Extreme cold may cause frost-bite; exposure to the sun, sun erythema, sun headache, and symptomatic fever; a

hot atmosphere, heat-exhaustion; prolonged residence in hot moist climates vague, ill-defined conditions of debility; residence in a dry cool climate a contrary effect; profuse sweating from heat of climate, prickly heat. But none of these states can with justice be regarded as disease.

This being so, it is natural to ask: In what way do tropical influences affect disease, as they undoubtedly do; and why should it be that some diseases are peculiar to tropical climates, or are specially prevalent in such climates?

Speaking generally, the natives of tropical countries are not injuriously affected by the meteorological conditions of the climates they live in, any more than are the inhabitants of more temperate climates; their physiological activities are attuned by custom and habit to the conditions they were born into. The European, it may be, on his first entering the tropics, and until his machinery has adjusted itself to the altered meteorological circumstances, is liable to slight physiological irregularities, and thus more especially if he persist in the dietetic habits appropriate to his native land. A predisposition to certain diseases, and a tendency to degenerative changes, may be brought about in this way; but acute disease, with active tissue change, is not so caused. In the tropics, as in temperate climates, in the European and in the native alike, nearly all disease is of specific origin. It is in their specific causes that the difference between the diseases of temperate climates and those of tropical climates principally lies.

Modern science has clearly shown that nearly all diseases, directly or indirectly, are caused by germs. It must be confessed that although in many instances these germs have been discovered, in other instances they are yet to find; nevertheless, their existence in the latter may be confidently postulated.

Germs are organised and living beings, and, like all living things, demand certain physical conditions for their well-being One of these conditions is a

certain temperature; another is certain media; and a third is certain opportunities.

In the majority of instances disease germs are true parasites and therefore to keep in existence as species require to pass from host to host. If, during this passage from host to host, the temperature of the transmitting medium be it air, water, or food—be too high or too low for the special requirements of the germ in question, that germ dies and ceases to be infective. In this way may be explained the absence from the tropics of a class of directly infectious diseases represented by scarlet fever, and the absence from temperate climates of a similar class of diseases represented by dengue. In the one case, during the short passage from one human being to another, tropical temperature is fatal to the air-borne germ; in the other the lower temperature of higher latitudes has the same effect.

In another type of disease, of which tropical scaly ringworm (*tinea imbricata*) is an excellent example, the germ vegetates on the surface of the body and is thus exposed to the vicissitudes of climate. One of the requirements of the germ referred to is a high atmospheric temperature and a certain degree of moisture. Given these it flourishes; remove these and it dies out, just as a palm tree or a bird of paradise would die on being transferred to a cold climate.

Many diseases require for their transmission from one individual to another the services of a third and wholly different animal. The propagation and continued existence of the disease will depend, therefore, on the presence of this third animal. If this be a tropical species, the disease for whose transmission it is necessary must necessarily be confined to the tropics. The third or transmitting animal operates in one of several ways. Thus in "fly disease," the protozoal organism which is the direct cause of the disease is carried from one animal to another on the mandibles of the tsetse fly. Consequently, unless the passive *rôle* of the tsetse fly is intentionally

imitated by man, the disease is not found outside what is known as "the fly belt," the geographical limits of which are very circumscribed, depending, among other things, on tropical conditions. Similarly, although on a somewhat different principle, the geographical range of filariasis is determined by that of special species of mosquito which ingest and act as intermediate hosts to the filaria, and, so to speak, prepare it for entrance into its definitive host—man. The distribution of a large number of animal parasitic diseases depends in this way on the distribution of the living inoculating agency, as in "fly disease," or of the intermediate hosts, as in filariasis. When this third animal happens to be a tropical species, the disease it subtends, so to speak, is, in natural conditions, necessarily tropical also.

Certain diseases are common to man and the lower animals. If these latter happen to be tropical species the opportunities for man to contract the common disease are most frequent, or are only found, in the tropics. Such, most probably, are some of the tropical ringworms. Such, I incline to believe, is malaria.

Certain parasites are so organised that before re-entering man they must pass a part of their lives as free organisms in the outer world, where they require a relatively high temperature for their development. Such parasites, therefore, and the diseases they give rise to, must necessarily be tropical or sub-tropical. The ankylostomum duodenale and ankylostomiasis is an instance in point.

There is a class of intoxication diseases which depend on toxins generated by germs whose habitat is the soil, water, or other external media, and whose germs do not enter the human body as a necessary feature in their life-histories, although their toxins may. The yeast plant and its toxin, alcohol, and the disease it causes, alcoholism, is the most familiar example of this. Such, too, are ergotism, pellagra, and, perhaps, lathyrism. The beriberi germ, its toxin

and beriberi, is probably another. These germs require certain temperatures and certain media ; consequently the diseases they produce have a corresponding geographical range. If one of these conditions be a high temperature, the disease, as in the case of beriberi, is a tropical one.

Lastly, I can conceive, and believe, that there is another and less directly-acting set of conditions influencing the distribution of disease, conditions which as yet have been ignored by epidemiologists, but which, it seems to me, must have an important bearing on this subject. Disease germs, their transmitting agencies, or their intermediate hosts, being living organisms, are, during their extra-corporeal phases, necessarily competing organisms, and therefore liable to be preyed upon, or otherwise crushed out, by other organisms in the struggle for existence. The malaria parasite is absent in many places in which, apparently, all the conditions favourable for its existence are to be found in perfection. Why is it not found there, seeing that it must certainly have been frequently introduced? I would suggest that in some instances this, and other disease germs, or the organisms subtending them, are kept under by natural enemies which prey on them, just as fishes prey on and keep down water-haunting insects, or as mice do humble-bees. The geographical range of such disease germs, therefore, will depend, not only on the presence of favourable conditions but, also, on the absence of unfavourable ones. Herein lies a vast field for study, and one which, as yet, has not been touched on by epidemiologists.

In these and similar ways the peculiar distribution of tropical diseases is regulated. The more we learn about these diseases the less important in its bearing on their geographical distribution, and as a direct pathogenic agency, becomes the *rôle* of temperature *per se*, and the more the influence of the tropical fauna.

It is evident from what has been advanced that the

student of medicine must be a naturalist before he can hope to become a scientific epidemiologist, or pathologist, or a capable practitioner. The necessity for this in all departments of medicine is yearly becoming more apparent, but especially so in that section of medicine which relates to tropical disease. This is further accentuated if we reflect that, although we do know something about a few of the tropical diseases and their germs, there must be many more tropical diseases and tropical disease germs about which we know absolutely nothing Who can doubt that just as the fauna and flora of the tropical world are infinitely richer in species than those of colder climates, so there is a corresponding distribution in the wealth and poverty of pathogenic organisms; and that many, if not most, of the tropical diseases have yet to be differentiated? Opportunities and appliances for original pathological study are, from circumstances, too often wanting to the tropical practitioner; but, in this matter of the ætiology of disease, he certainly enjoys opportunities for original research and discovery far superior in novelty and interest to those at the command of his fellow inquirer in the well worked field of European and American research.

In the following pages I have included certain cosmopolitan diseases, such as leprosy and plague, diseases which, properly speaking, do not depend in any very special way, or necessarily, on climatic conditions. They have been practically ousted from Europe and the temperate parts of America by the spread of civilisation, and the improved hygiene that has followed in its train, and are now practically confined to tropical and sub-tropical countries, where they still survive under those backward social and insanitary conditions which are necessary for their successful propagation, and which are more or less an indirect outcome of tropical climate.

TROPICAL DISEASES.

SECTION I.—FEVERS.

CHAPTER I.

MALARIA.

Definition.—A protozoal organism of warm climates, which, although ordinarily living in external nature, is capable of becoming parasitic and of multiplying in man. It gives rise to fever—usually of a periodic character, anæmia, enlargement of the spleen, and the deposit of a black pigment in the viscera and elsewhere. Certain of its parasitic phases are amenable to quinine.

The malaria parasite.

Its importance.—This organism is by far the most important disease agency in tropical pathology. Not only does it give rise to grave and sometimes fatal fevers, but, in consequence of its prevalence, of its anæmiating and debilitating influences, and of its tendency to cause congestion of the abdominal viscera, it undermines the health of millions; predisposing them to other diseases which it complicates and aggravates; impairing their powers of resistance and repair; and otherwise unfitting them for the active business and enjoyment of life. Directly and indirectly it is the principal cause of morbidity and death in the tropics and sub-tropics.

The plasmodium malariæ the cause of malarial disease.—It is now practically certain that the presence and proliferation in the blood of this parasite,

discovered by Laveran in 1880, and conveniently known as the *plasmodium malariæ**, is the cause of what was formerly, and is still, known as "malarial disease." The following are the principal reasons for this belief:—

1. The occurrence of the plasmodium in the blood is always, sooner or later, associated with the clinical phenomena of malarial infection.

2. Malarial fever throughout, or at one time or another during its course, is practically invariably associated with the presence of this parasite in the blood.

3. The phases of malarial fevers bear a definite relation to the phases of the life cycle of the parasite.

4. Those absolutely characteristic features of malarial disease—melanæmia and malarial pigmentation of viscera—are fully accounted for by the melanin-forming property of the plasmodium.

5. Intravenous injection of blood from a case of malarial infection—that is, of blood containing the plasmodium—is generally, after an incubation period of eight to twelve days, followed by an attack of malarial fever and by the appearance of the plasmodium in the blood of the person injected.

6. The administration of quinine, which brings about the cessation of the clinical symptoms of acute malarial infection, rapidly causes most phases of the plasmodium to disappear from the blood.

Hitherto all attempts to cultivate the parasite, whether in the ordinary culture media or inside the bodies of the lower animals, have failed. Until this has been successfully effected, and until experimental infection of man from a pure culture has been followed by typical malarial disease, absolute proof of

* The malaria parasite is not a plasmodium in the zoological meaning of the word. To this extent the introduction of the name *plasmodium malariæ* is to be regretted. However, of the many names given to the organism this is the one most usually employed; and as it is now in such general use, I have thought it advisable to adopt it, notwithstanding its inaccuracy in a scientific sense.

the causal relationship of the parasite to the disease may be said to be wanting; short of this, however, proof is complete, and, as already remarked, the plasmodium may with confidence be accepted as the cause of malaria.

Necessity for a practical knowledge of the plasmodium.—For the full understanding, therefore, of the ætiology and pathology of malaria, apart from the very practical consideration of diagnosis, it is of the first importance that the student should be thoroughly familiar with what is known of the life-history of the plasmodium, and with the various appearances it assumes in the blood. To enable him to acquire this knowledge it is absolutely necessary that he should acquaint himself with, and practise himself in, the art of demonstrating the parasite.

MORPHOLOGY AND HISTOLOGY OF PLASMODIUM MALARIÆ.

Its zoological affinities.—Zoologically, the plasmodium is placed by most recent authorities among the sporozoa. It is closely allied to the coccidia.* Like these, for the greater part of its known life, it is an intra-cellular parasite, its special habitat so far as man is concerned being the red blood corpuscles. Many of the other vertebrata are affected by similar, though specifically distinct, parasites; that of man, so far as known, is special to himself.

Of the human plasmodia there are several varieties, possibly species. The distinctive characteristics of each of these will be detailed farther on. The following brief description is confined to what may be regarded as the generic features common to all.

* Recent observations, particularly those of R. Pfeiffer and of Simond (*Ann. de l'Inst. Pasteur*, July 27, 1897), by showing that many coccidia possess a double life cycle—one adapted for the multiplication of the parasite in the original host, and one adapted for its transmission to fresh hosts—have thoroughly established the close relationship, previously merely conjectured, of the plasmodium to this order of sporozoa.

Its three phases.—The plasmodium, like all true parasites, must be adapted not only for a life inside its host but also, in order that its continuance as a species may be assured, for a passage from one host to another. Consequently it exhibits two distinct phases—an intra-corporeal or human phase, and an extra-corporeal phase. Clinical observation makes it certain that there is yet another phase—the latent phase.

Intra-corporeal or human cycle.

Each variety or species of the intra-corporeal plasmodium has its special and more or less definite life-span of twenty-four hours, of forty-eight hours, or of seventy-two hours.

On examining malarial blood towards the end of one of these cycles, an hour or two before the occurrence of one of the paroxysms of the characteristic periodic fever it induces, the parasite may be recognised as a pale, somewhat ill-defined disc of protoplasm, occupying a larger or smaller area within a proportion of the red blood corpuscles (Fig. 1, *a*).

Fig. 1.—Evolution of the benign tertian parasite, unstained. (*Compiled from Thayer and Hewetson.*)

Scattered through this pale body are a number of particles of intensely black or reddish-black pigment—melanin.

By repeating his examinations and making them at short serial intervals, the observer is enabled

to ascertain that certain changes systematically occur in this disc of pigmented protoplasm. He will find that after a time the scattered pigment particles collect into little groups, sometimes into radiating lines. These pigment groups subsequently concentrate into one or two larger and more or less central blocks, around which the pale protoplasm of the plasmodium arranges itself in minute segments which finally acquire a globular form and appear as well-defined spherules—spores (Fig. 1, *b*, *c*, *d*). The including blood corpuscle then breaks down and the spores, none of which contain pigment, fall apart and, along with the clump or clumps of melanin, become free in the liquor sanguinis (Fig. 1, *e*). The phagocytes now quickly absorb the melanin and many of the spores. A proportion of the latter, however, escape the phagocytes and attach themselves to other blood corpuscles which, in some unknown way, they contrive to enter (Fig. 1, *f*). In the interior of these newly infected corpuscles the young parasites exhibit active amœboid movement, shooting out and retracting long pseudopodia, and growing at the expense of the hæmoglobin (Fig. 1, *g*). This substance they assimilate, converting it into the pale protoplasmic material constituting the mass of the parasite, and into the melanin particles (Fig. 1, *h*, *i*). As the parasite becomes larger its amœboid movements gradually slow down until all motion finally ceases; just before sporulation (Fig. 1, *j*), beyond slight translation movement of the pigment particles, the plasmodium is passive.

By staining with methylene blue, the plasmodial spore (Fig. 2, *b*, *c*, *d*) is found to consist of a minute, deeply tinted nucleolus surrounded by an unstained (in its early stage not very apparent) vesicular nucleus, and this again by a somewhat lightly tinted covering of protoplasm. After the spore has entered a blood corpuscle (Fig. 2, *e*), staining shows that the vesicular nucleus has become larger and more distinct, that the protoplasm has

increased in bulk, and that the deeply stained nucleolus, which is sometimes double, has come to lie eccentrically in the nucleus. On account of the relatively large size of the unstained nucleus, the eccentric position of the deeply stained nucleolus, and the narrow rim of stained protoplasm, the younger

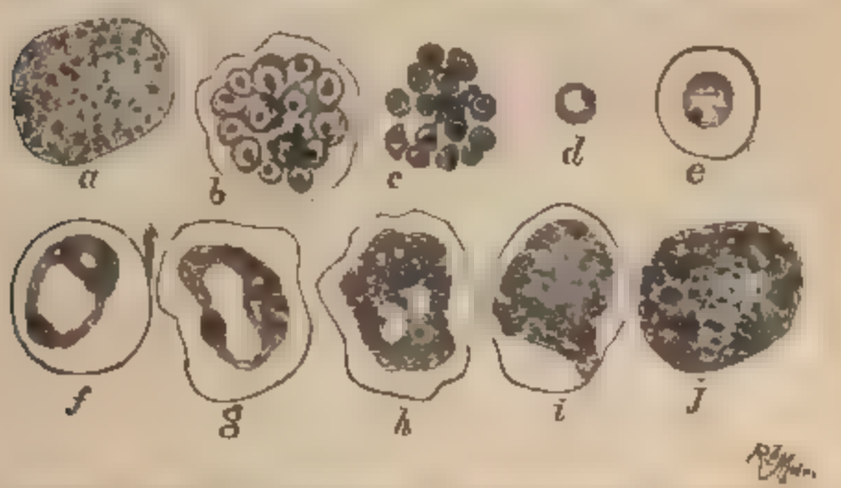

Fig. 2.—Evolution of the benign tertian parasite, stained with methylene blue. (*Compiled from Mannaberg.*)

parasites when stained look like so many minute blue signet rings stuck on to the blood corpuscles. As the parasite grows and approaches maturity the nucleolus disperses and the vesicular nucleus becomes less distinct (Fig. 2, *f*, *g*, *h*, *i*); finally, just before sporulation, both nucleus and nucleolus have ceased to be distinguishable (Fig. 2, *j*, *a*). Apparently at this stage these elements, in some undetermined way, become fragmented or diffused throughout the protoplasm. Later the nuclear elements reappear as numerous, minute, scattered nucleoli; and it is around these that the protoplasm of the now segmented parasite arranges itself to form the spores (Fig. 2, *b*, *c*). The vesicular nucleus does not usually appear in the spores until after they become free in the liquor sanguinis (Fig. 2, *d*).

The melanin particles, so characteristic of the malaria germ, occur either in dust-like specks, in

coarse grains, in short rods, or aggregated into dense clumps. Until the concentration of pigment which precedes sporulation takes place the particles are scattered, being located principally in what, were we to regard the plasmodium as an amœba, might be described as the ectosarc.

Such is a brief account of the structure and life cycle of one phase of the plasmodium. From it we may understand how the parasite maintains itself and multiplies inside the human body. It does not explain, however, two important features in the life of the plasmodium, which analogy and observation clearly indicate—namely, latency and the life of the parasite outside the human body.

Latent phase.—It is a well-established fact that, concurrently with the subsidence of acute clinical symptoms, the plasmodium may disappear from the general circulation and pass into a latent condition. This it does either spontaneously or as a result of the administration of quinine. As to the organ or tissue it selects, or as to its appearance and structure during this state of latency, or as to the exact conditions which cause it once more to resume active, propagating, circulating life, nothing whatever is known. This much, however, we do know—namely, that physiological strain or vital depression in the host tend to bring about conditions which break up, and that quinine and vital vigour tend to bring about conditions which favour, latency.

Extra-corporeal cycle.—As it is unreasonable to suppose that an organism which propagates so actively in the human body has no opportunity, either by passing from one host to another or in other ways, of continuing its species, we are forced to conclude that some provision must exist in the economy of the parasite that enables it to leave and enter successive hosts. And as malaria is well known to exist in many places where man is rarely found, it follows that provision must also be made in the economy of the plasmodium for a life, either free or parasitic, which is not

dependent on man. The problems suggested by these considerations are: First, how does the malaria parasite leave the human body to get a chance of following an extra-corporeal life; second, what is this life; and, third, how does the parasite enter the human body?

I have advanced a theory in explanation of these points, and, together with Surgeon Major Ronald Ross,

Fig. 3. Malaria parasite: flagellated body.

I.M.S., have brought forward a considerable body of fact and argument in its support. I shall describe this theory, which may or may not be correct, because it seems to articulate logically many well ascertained facts in the life-history of this important parasite, and because it gives a certain completeness to our conception of the subject. Before doing so it will be necessary to point out certain additional features or phases of the plasmodium, not yet alluded to.

The flagellated body.—When fresh malarial blood is examined some time after it has been mounted it is no unusual thing to see what is known as the

"flagellated body" (Fig. 3).* Varieties of this body are found in all forms of plasmodial infection, in the case of the corresponding parasites of the lower warm-blooded animals as well as in the forms special to man. It is a strange-looking, octopus-like creature, with long, actively moving arms. Though composed of the same materials—namely, colourless protoplasm and dark melanin granules—it differs from the ordinary

Fig. 4. Malaria parasite: flagellated body with free-swimming flagellum.

parasite inasmuch as it is not intra-corpuscular. The long, whip-like arms, numbering from one to six, or even more, are usually designated *flagella*. They are exceedingly delicate and pliant filaments; often difficult to see, not only on account of their delicacy but also on account of the rapidity of their movements. Sometimes bulbous at the free extremity, sometimes presenting one or more swellings in their continuity, the flagella are three or four times as long

* The expressions "flagellated body" and "flagellum," applied to this phase of the malaria parasite are somewhat misleading. The flagella of the malaria parasite are in no sense analogous to the flagella of the flagellata.

as a blood corpuscle is broad. At first they are attached to the periphery of the pigmented central, more or less spherical, body, which is about half the diameter of a red blood corpuscle. The movements of the flagella are so vigorous that, without seriously injuring them, they double up and distort temporarily those corpuscles with which they chance to come in contact. Occasionally it may be observed that one

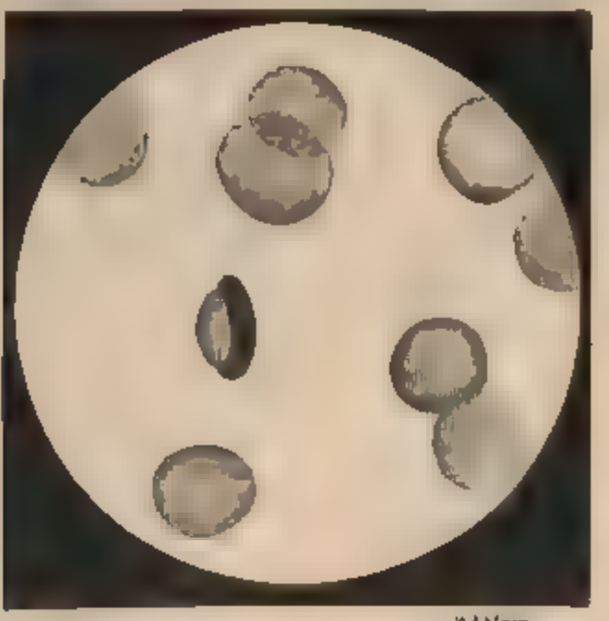

Fig. 5. Malaria parasite: the crescent body, stained. (× 1000.)

or more of the flagella break away from the central sphere and swim free in the blood (Fig. 4), remaining active for a considerable time—several hours perhaps before they finally vanish.

Careful observation shows that the flagellated bodies are developed from two forms of the intra-corpuscular parasite—namely, in certain types of malarial infection from what is known as the "crescent body"; in other types from certain large intra-corpuscular plasmodia. It is of importance to bear in mind that they are never seen in newly-drawn blood, and that they come into view only after the slide has

been mounted for some time—ten to thirty minutes or even longer, according to circumstances.

The crescent body.—The shape, size, and structure of the crescent body can best be comprehended from the illustration (Fig. 5). The principal features to be noted are its very definite mathematical shape; the probable existence of a delicate limiting membrane; the presence of melanin particles usually about the centre of the parasite, though sometimes nearer one end; and a peculiar bow-like and exceedingly delicate line that, springing from the horns of the crescent, bridges its concavity. Manifestly this bow represents the outline of the remains of the blood corpuscle in which the parasite had developed. In many instances, especially in stained specimens, the continuation of the red blood corpuscle can be distinctly traced around the convexity of the crescent. This circumstance—together with the fact that the material included by the bow and also occasionally seen as a delicate, sometimes slightly jagged, rim around the convexity of the crescent, gives the staining reactions of hæmoglobin—proves that this form of the malaria parasite, like the ordinary plasmodium, is also intra-corpuscular. Slight differences, particularly as regards the sharpness or obtuseness of the horns, occur; but, on the whole, the crescents are very uniform in appearance. Very rarely twin or double crescents—that is, two crescents in one corpuscle—are encountered (Fig. 6). Although the origin of the crescent body has not been conclusively explained, it seems to me that Mannaberg's suggestion that it is the result of the conjugation of two ordinary

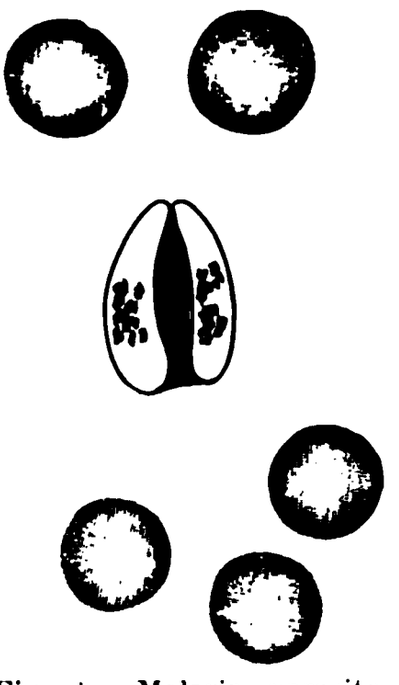

Fig. 6.—Malaria parasite: twin crescents.

plasmodia—a syzygium, in fact—in a doubly infected blood corpuscle, is likely to prove the true one.

Formation of the flagellated body.—Although there may be doubt about its mode of origin, it can be said with confidence that the destiny of the crescent has been determined. This destiny is the formation of the flagellated body belonging to the special type of plasmodial infection in which the crescent occurs (Fig. 7, *b*). If a number of crescent bodies are kept for a time under observation on the microscope slide, a certain proportion of them will be seen slowly to undergo change of shape, gradually becoming converted first into oval bodies and then into spheres (Fig. 7, *b*, *c*), whilst the remains of the enclosing blood corpuscle fall to pieces or melt away. At first the pigment particles, both in the crescent, in the oval body, and in the sphere, are motionless and central—more rarely eccentric. By and by these particles tend to arrange themselves as a ring, lying in contact with the inner surface of what may be a very fine, invisible membrane, and occupying the central third of the sphere, and forming, as it were, a small central sphere within the larger sphere. After a time the pigment particles begin at first slowly and intermittently, afterwards more energetically to dance about. As the movement of the pigment increases in rapidity and energy, the entire sphere seems to partake in the agitation—to quiver,

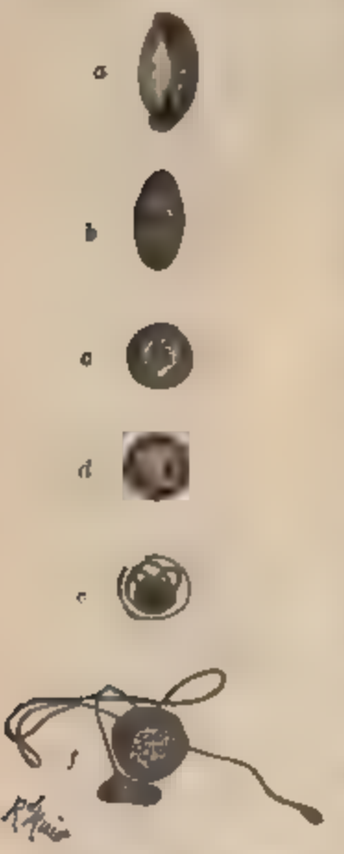

Fig. 7. Malaria parasite: evolution of the flagellated body from the crescent parasite.

to change form, and to be jerked about as by some unseen force. The pigment particles may now become diffused through the general mass of the sphere (Fig. 7, *d*), or they may not. Whether this does or does not happen, the agitation of the sphere now becoming intense, one or more flagella are suddenly shot out from its periphery, and begin at once

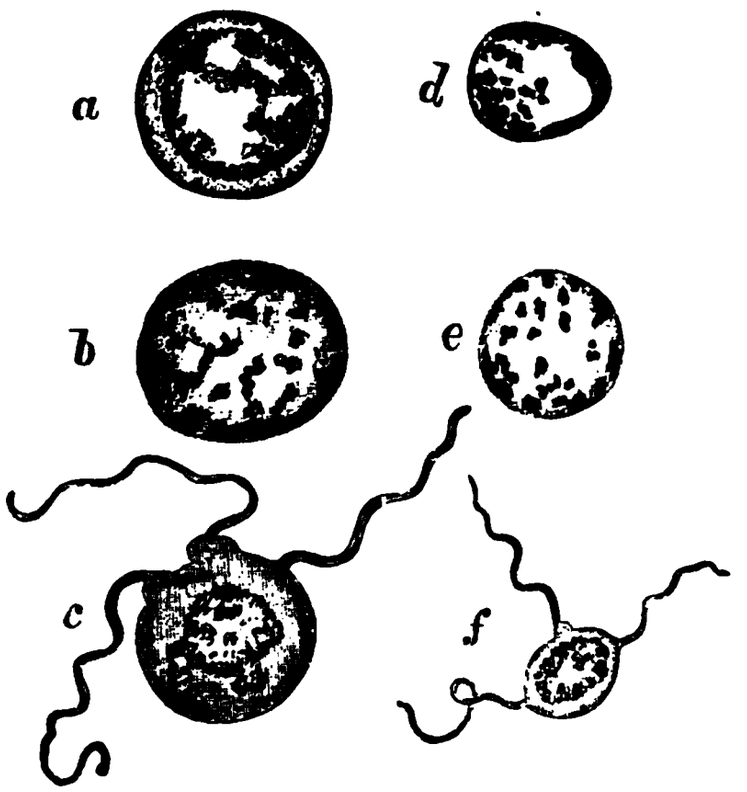

Fig. 8.—Evolution of the flagellated body in the tertian (*a*, *b*, *c*) and quartan (*d*, *e*, *f*) parasites. (*Compiled from Thayer and Hewetson.*)

to indulge in characteristic waving, lashing movements (Fig. 7, *f*).*

The flagella, if they do not succeed in breaking away as already described, may continue to move for an hour, or even longer—that is, if the flagellated body is not engulfed by a phagocyte, an occurrence very frequently witnessed. Finally, they slow down, cease to move, curl up perhaps, and then gradually

* Careful focussing, especially of stained crescent-derived spheres, may sometimes show that for a short time before their eruption the flagella exist preformed inside the limiting membrane of the sphere (Fig. 7, *e*). Doubtless the agitated movements of the sphere are produced by the efforts made by the flagella to break through this membrane.

fade from view. Should the flagella succeed in breaking away, the remains of the flagellated body, consisting of pigment particles included in a small amount of residual protoplasm, tend to assume a somewhat spherical, passive form, the hitherto violent changes of shape, and the movement of the pigment ceasing almost abruptly.

In another variety of plasmodial infection certain bodies (Fig. 8, *a*, *d*), which look like ordinary full-grown intra-corpuscular parasites prior to the formation of spores, may sometimes be seen to slip out from their enclosing corpuscles (Fig. 8, *b*, *e*). If these escaped plasmodia are watched, in some instances the pigment they contain is seen to indulge in violent dancing movements, the body of the parasite being at the same time violently agitated and jerked about. Finally, flagella may be suddenly projected from the periphery of these plasmodia (Fig. 7, *c*, *f*), very much in the same way as the flagella are projected from the periphery of the crescent-derived sphere. Manifestly, these large spherical plasmodia and the flagellated bodies arising from them correspond to the crescent-derived sphere and crescent-derived flagellated body.

Ross has recently shown that, provided the blood containing the crescent body is prevented from coming in contact with the air as when the finger is pricked through vaseline, the evolution of the parasite does not proceed. He has further shown that if the droplet of blood is exposed to the air for a minute or two before being mounted on a slide, exflagellation is markedly encouraged. Similarly, Marshall has shown that by mixing the blood with a trace of water exflagellation is also favoured. I find that by combining these methods, namely, exposure to the air with slight aqueous admixture, as by breathing on the slip before applying the cover-glass, it is generally easy to procure quickly specimens of the flagellated body from crescent-containing blood. Probably, although I have not experimented with this object in suitable cases, flagellation will be favoured in

the non-crescent forming plasmodia by the same means.

Function and nature of the flagellated body.—From the fact that the flagellated body does not come into existence until the blood has left the vessels—in other words, is outside the human body—I have ventured to suggest that the function of the flagellum must also lie outside the human body; and because the flagella are formed from plasmodia of large size and apparently mature, and for other reasons, I have also suggested that the flagella are flagellated spores, the extra-corporeal homologues of the intra-corporeal spores; in fact, that the flagellated body constitutes the first phase of the extra-corporeal life of the plasmodium.

The mosquito considered as the extra-corporeal host of the plasmodium.—Further, as the plasmodium whilst in the circulation is always enclosed in a blood corpuscle and is therefore incapable of leaving the body by its own efforts, and as it is never, so far as known, extruded in the excreta, I have suggested that it is removed from the circulation by some blood-eating animal, most probably by some suctorial insect common in the haunts of malaria. This insect, as Laveran has also suggested, I believe to be the mosquito*; an insect whose habits seem well adapted for such a purpose, and whose distribution in nature would seem to satisfy the demands entailed by the well-ascertained habits of malaria.

In ordinary liquid slides of crescent-containing malarial blood, only a very small percentage of crescents proceed to flagellation; by far the larger proportion never change form, or proceed merely to the oval or, at the most, to the spherical stage. In support of the theory I advocate Surgeon-Major Ross, I.M.S., proved that it is otherwise with the crescents ingested by mosquitoes fed on malarial blood.

* For a fuller statement of the facts and arguments bearing on this theory the reader is referred to the writer's Goulstonian Lectures, *Brit. Med. Journal*, March 14th, 21st, and 28th, 1896.

In such circumstances he finds—and I can confirm from inspection of his preparations the accuracy of his statements—that the crescents in the majority of instances become transformed into spheres (Fig. 9) and then into flagellated bodies, the flagella subsequently breaking away and becoming free in the stomach of the insect. This constancy of exflagellation in the mosquito's stomach cannot be accidental. I consider that the flagella—which, as already stated, are to be regarded as flagellated spores—are endowed with their peculiar shape and properties, in other words, with locomotive powers, in order that they may be able to pass from the blood in the mosquito's stomach to the tissues of the insect. I conjecture that the flagellum enters some cell of the mosquito and therein, like any gregarine or coccidium, becomes parasitic, growing and sporulating afterwards; just as the non-flagellated plasmodium enters, grows, and sporulates in the human blood corpuscle. The plasmodium, I hold, is an intra-cellular parasite both outside as well as inside the human body, and that when outside the human body it is parasitic in the mosquito.

Fig. 9. Earlier stages of the evolution of the crescent body in the mosquito.

In further support of this hypothesis Ross's most recent observations, to be alluded to presently, may be quoted. Certain it is that the phenomena of exflagellation are no mere freak of nature, and certain it is that they have direct reference to the welfare of the organism exhibiting them. The details I have ventured to fill in may not be correct in every particular, but the principle must be conceded.

I have further conjectured that the continuation and multiplication of the plasmodium outside the

human body is secured by the passage of the mosquito-bred plasmodial spore into the larvæ of the same insect. The mosquito generally dies in the water beside the eggs she has deposited. When the eggs are hatched the young larvæ commonly devour the body of their parent and, consequently, her parasites. Moreover, being very voracious, the larvæ eat any organic matter they come across. We can easily understand from this in what way parasites from the mosquito may get access to the mosquito's offspring. On the infected larvæ becoming mature insects the

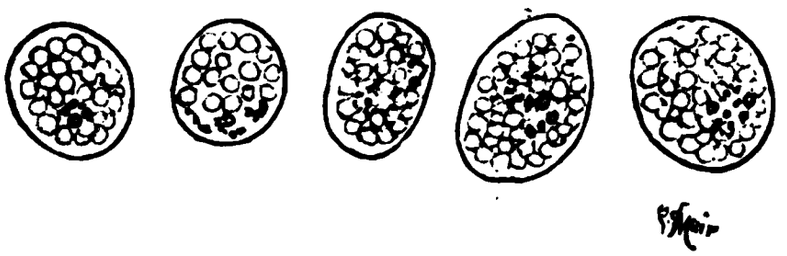

Fig. 10.—Pigmented cells from stomach wall of mosquito.

plasmodia they have swallowed continue, I conjecture, to develop. These insects, in their turn, infect their larvæ, and so on. Continuation and multiplication of the plasmodium outside the human body is in this way secured. Man, I conjecture, may become infected by drinking water contaminated by the mosquito; or, and much more frequently, by inhaling the dust of the mud of dried-up mosquito-haunted pools; or in some similar way.

It seems to me that this hypothesis explains many facts in the ætiology of malarial infection. If true, it would account for the long-recognised relationship of malaria to swamps; for the influence of drainage and of deep flooding in rendering malarial lands salubrious; and for many other points in the ætiology of paludism. I do not maintain that this mosquito hypothesis has as yet been thoroughly proved, but I do maintain that it is so probable, and of a character so important, from both a scientific and practical point of view, that every effort should be made to establish or confute it.

Another and plausible interpretation of the function of the flagellum has (*Lancet*, November 13th, 1897), been advanced by MacCallum of the Johns Hopkins Hospital; an interpretation, moreover, entirely compatible with the mosquito hypothesis. MacCallum has found that an endocorpuscular pigmented parasite (*halteridium* of Labbé) occurring in an American crow, and analagous to the plasmodium of man, when it has attained its adult size is, in certain instances, extruded from the including corpuscle. After escape it assumes a spherical form, in some instances having a granular and opaque appearance, in other instances being hyaline and transparent. After a time the hyaline halteridia project flagella which, breaking away from the parent sphere, accumulate around and vigorously seek to enter the granular, non-flagellated, free halteridia. Ultimately one of the flagella succeeds in effecting an entrance, causing considerable agitation among the pigment particles. The halteridium, being thus impregnated, as it were, slowly changes form, becoming elongated into a pigmented, spindle shaped body or vermicule, which presently begins to move about through the blood traversing red and white blood corpuscles indifferently and continuing active for a considerable time.

MacCallum further states that in blood from a woman, in whom the crescent form of the malaria parasite was unusually abundant, he twice witnessed a somewhat similar phenomenon. He saw a flagellum enter a crescent-derived sphere, agitate the pigment and spin round the central portion of the parasite The sphere, however, underwent no further change of shape, nor anything like development into a vermicule. It is conceivable, however, that under more natural conditions some such transformation might occur, indeed, if MacCallum's observations are correct, analogy would indicate that some such transformation does occur.

Ross has (*Brit. Med. Journ.*, December 18th, 1897) observed certain pigmented cells (Fig. 10) in

the wall of the stomach of a peculiar species of mosquito which he had fed on crescent-containing blood. From their appearance, and from the circumstances in which they occurred, these cells were evidently, or in all probability, associated in some way with the malaria parasite; indeed, it seems highly probable that they contained the parasite, for their pigment was, so far as the microscope entitled him to infer, in every respect similar to the malarial pigment. Assuming that these cells were, or that they contained, the malaria parasite, it is somewhat difficult to understand from what source their pigment was derived if, as conjectured, the flagellum, which is always non-pigmented, were the direct infecting agency. But in the light of MacCallum's discovery it can be readily understood how, if certain of the crescent-derived spheres were impregnated by free flagella in the stomach of the mosquito and subsequently became travelling pigmented vermicules like those of *halteridium*, they could carry with them into the cells of the stomach wall of the insect their melanin granules.

Bignami conjectures that the plasmodium is conveyed to man by the bite of the mosquito, its proboscis carrying malaria germs acquired from the water or soil of a malaria-infested locality. Experiment has not encouraged this idea.

Crescents, spheres, and flagellated bodies regarded as degenerated parasites.—Though strongly opposed to the view, I consider it right to mention that many high authorities—Marchiafava, Bignami, Blanchard among them—regard the malaria crescent, sphere, and flagellated bodies as being degenerated, dead, or moribund plasmodia. In support of this opinion they adduce the fact that the red blood corpuscles, when heated, sometimes project waving filaments something like flagella. They also state that the nucleus of the parasite has not been shown to take any part in the formation of the flagella, and that similar phenomena accompany the death of other

protozoa. Grassi and Feletti maintain that the crescent is a distinct and independent species of parasite, quite different and in no wise, except by accidental concurrence, connected with the ordinary intra-corpuscular plasmodium. Recent advances in our knowledge seem to me to render such views untenable.

Preparation of blood for detecting the plasmodium.—For a thorough appreciation of the principles on which blood examinations for the demonstration and study of the plasmodium should be conducted, it is necessary to bear in mind that the parasite is intra-corpuscular. To see it with the microscope, therefore, it is necessary, particularly for the beginner, so to dispose the corpuscles in the preparations that a proportion of them shall lie flat

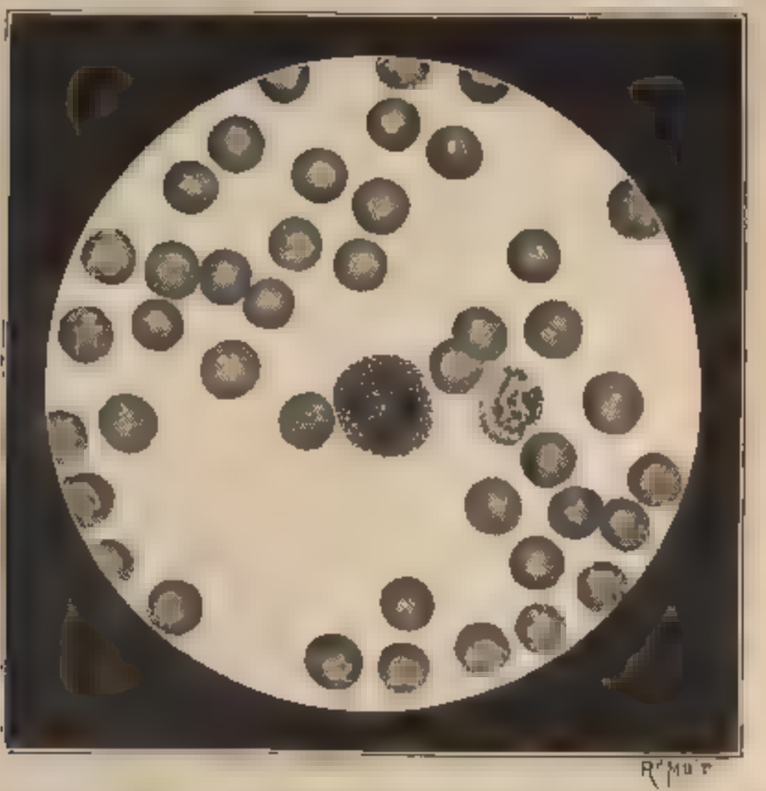

Fig. 1.—Micro-photograph showing the necessary disposition of blood corpuscles in a slide for examination for the plasmodium. To the right of the white blood corpuscle in the centre of the field, a red blood corpuscle three fourths filled with a tertian benign parasite is visible. (*From micro-photogram by Dr. Loos.*)

on the slide, in a single layer, and presenting their surfaces and not their edges to the observer (Fig. 11). It is mainly from ignoring this fundamental principle that so many fail to find the plasmodium.

To secure this disposition of corpuscles the following procedure, the smallest detail of which must be scrupulously carried out, is recommended.

Thoroughly cleanse with alcohol three or four thin cover-glasses and as many slips, and cover them immediately with some convenient vessel so as to protect them from the minutest particle of floating dust. After lightly ligaturing one of the patient's finger-tips, cleanse it with alcohol and dry it. Prick the congested finger pad with a clean needle, and wipe away the first drop of blood that exudes. Then gently, with finger and thumb, squeeze the finger pad and express a second minute droplet of blood; this should be very small—no larger than a pin's-head. Touch the droplet lightly with the centre of a cover-glass, taking care that the latter does not come into contact with the skin, and immediately lay it on the slide. No pressure should be used to cause the blood to spread out. If glasses and finger are quite clean, the blood will at once run out in a very fine film.

Several preparations should be made, the requisite blood being obtained by renewed gentle compression of the finger-tip.

After waiting a few minutes to allow the blood to spread out completely between the glasses, it is well to ring the preparations with vaseline; this will effectually stop all movement, all evaporation of the blood, and, consequently, over-compression and crenation of the corpuscles, and will thereby greatly facilitate examination.

In preparing slides care should be taken to sterilise the needle employed, otherwise grave accidents might occur. It is of course unnecessary to sterilise the slides used.

On holding a successful preparation up to the light, one or more areas, each made up of three zones,

the different zones shading into each other, can be made out by the naked eye. Each such area includes a peripheral zone of a reddish tinge, a middle zone having a somewhat iridescent look, and a central zone absolutely devoid of colour. Successful preparations may be recognised by the presence of these zones. Preparations not exhibiting this appearance should be rejected, it is waste of time to examine them.

On examining successful preparations with the microscope, it will be found that the central zone or area contains few or no blood corpuscles. This zone may be designated the "empty zone." Proceeding outwards from this we come on an area occupied by scattered, isolated, compressed, and much-expanded corpuscles; this zone I shall designate the "zone of scattered corpuscles." Farther out the corpuscles become more numerous and less expressed (Fig 11) and, gradually, as we trace the slide still farther outwards, the corpuscles are found approximated to each other until, finally, the peripheries of the corpuscles are mostly in touch; this zone I shall call the "single-layer zone." Farther out the corpuscles, though still lying flat, are found to overlap each other or are piled one on the top of the other; this zone I shall call the "zone of heaped up corpuscles." Beyond this zone the corpuscles are arranged in rouleaux, "the zone of rouleaux." At the extreme margin of the preparation the corpuscles tend to break up and run together so as to form a narrow border of free hæmoglobin, the individual corpuscles, perhaps, being indistinguishable; this I shall call the "zone of free hæmoglobin." Each of these zones should be studied, for each carries special information about the plasmodium.

Microscopical examination.—The beginner will save time if he gets someone who is familiar with the necessary technique and with the appearance of the parasite in the blood to give him one or two lessons. Accuracy and quickness can be acquired only by practice. It is a good plan to practise preparing films from one's own blood.

The examination is best conducted with $\frac{1}{12}$ of an inch oil immersion lens, a rather low eyepiece, a substage condenser, and not too dazzling an illumination.

It is not always possible to choose, but, if practicable, a case of quartan infection should be selected for examination in the first instance. Failing a quartan, a well-defined benign tertian infection might be chosen. Failing either of these, a long-standing case of recurring malaria with marked cachexia will afford the next best opportunity. It is best to examine the patient's blood just before or at the time of rigor. In quartans and benign tertians, at the time named, there should be little difficulty in discovering large plasmodia; in their case attention is called to the relatively large parasites by the abundance of coarse pigment which they contain. In the blood of malarial cachectics with recurring febrile attacks it is generally an easy matter to find crescents and crescent-derived spheres, as this form of the parasite is of considerable size, carries abundance of pigment, and possesses a very definite and striking shape.

When the beginner has learnt to recognise one form of the parasite, he will begin to appreciate what sort of body he has got to look for, and thereafter should be able to educate himself, and to pick out the smaller and all the other forms.

In proceeding to make his first examination of a liquid blood slide, the beginner, in the first instance, should confine his attention to the "single-layer zone." Field after field of this he must pass in review, carefully scrutinising the interior of every blood corpuscle, every leucocyte, and every pigmented body even though it be not included in a corpuscle. He must not expect to find parasites in every corpuscle or even in every field; and he certainly must not expect, as the beginner usually does, to find in every slide the beautifully regular sporulating form or "rosette body," or the weird-looking flagellated body made familiar to us by so many

illustrations. Such bodies, though really present somewhere and in some form at one time or another in every case, are among the least commonly encountered of the many phases of the plasmodium; they are met with only under very definite and not very constantly encountered conditions, and are not very often seen at an ordinary clinical examination.

In most cases the plasmodium is discovered in the first field or two examined; but in not a few instances dozens of fields may have to be scrutinised before a single parasite is encountered. Therefore no examination can be said to be complete, in a negative sense, until at least half an hour has been spent over several suitably prepared slides.

The forms of intra-corpuscular plasmodia most frequently met with have the appearance either of small specks of pale protoplasm, or of larger masses of pale protoplasm containing grains of black pigment. Close watching discovers that the former are endowed with active amœboid movement, and that they continually change shape and position in the affected corpuscles. As these movements are an important test of the parasitic nature of the body sought, they should be carefully looked for. These protoplasmic specks look like little washed-out smudges of dirty white paint, half hidden by the hæmoglobin; they are sometimes hard to see. Their parasitic nature can readily be determined by their movements; their soft, ill defined margins; and by the fact that they tend now and again, on first removal from the body, and permanently later, to assume the appearance of tiny white rings which show up very distinctly in the hæmoglobin of the corpuscle. These features readily distinguish them from the sharply defined, clear, motionless vacuole (Fig. 12). The other common forms the larger or smaller intra-corpuscular pigmented parasites occupy anywhere from a sixth to nearly the entire area of the affected corpuscles. They are recognised by their pale protoplasm; the black melanin particles sprinkled about or, if towards the

period of rigor, concentrated in their interior; and by their more or less active amœboid movements. In quartans and tertians, but especially in the former, sporulating rosette forms are seen occasionally.

Examination of blood for flagellated bodies.—When the student has become familiar with these appearances, and has thoroughly seized the fact that the sporulating forms are to be found only, or usually, at and just before or soon after the rigor stage of fever, he should endeavour to follow up the extra corporeal, or the initial steps of what, under natural conditions, I hold to be the mosquito stage of the parasite. So far as ordinary preparations permit, this phase is best studied in the zone of "heaped-up corpuscles" and in the "zone of rouleaux"; because in these zones the parasite, not being subjected to pressure, has more freedom to undergo its evolutionary change into the flagellated body.

In ordinary quartans and tertians the flagellated body is but seldom encountered. The best time to find them in such cases is during the hot stage of the fever. In cases of crescent infection flagellated bodies are much more frequently encountered as, in this form of malaria, they are more numerous and appear at any time of the clinical cycle, and perhaps for weeks after fever has disappeared.

In most cases of crescent infection the gradual evolution of the flagellated body from crescent through oval and sphere can, with patience, be easily followed.

Diagnostic value of the "zone of free hæmoglobin."—The zone of free hæmoglobin is of value as enabling the practical observer to pronounce very rapidly on the presence or absence of pigmented parasites in the blood. The relatively large quantity of blood in each field of this zone, and therefore the proportionally large number of parasites in any given field, lends itself to this, as does the fact that the black pigment shows up very distinctly in the homogeneous lake-coloured sheet of free hæmoglobin.

Phagocytosis and pigmented leucocytes.—Striking

examples of phagocytosis are often witnessed in the zones of heaped up corpuscles and of rouleaux. It will be found that so soon as a malarial parasite, whether spontaneously or as a result of pressure, escapes from the blood corpuscle in which it had developed, it becomes exceedingly liable to attack by the phagocytes. More especially is this the case with the flagellated organism; this body seems to have a powerful attraction for the phagocyte, which is often seen to travel long distances to attack it.

Pigmented leucocytes—that is to say, leucocytes containing grains or blocks of melanin—are very often encountered in all of the zones; they can best be seen in the single-layer zone during, or shortly after, fever. The leucocytes may sometimes be observed to swallow the pigmented centre of the broken-up sporulating bodies. Often they derive their pigment from the remains of some sphere or flagellated body which they have engulfed subsequently to the preparation of the slide. In peripheral blood the phagocytes are rarely, if ever, seen to attack the plasmodium so long as the parasite is inside a blood corpuscle.

Both the mono- and the poly-nucleated leucocytes may contain malarial pigment. Great care, however, must be exercised in drawing conclusions from the discovery of finding black material in these bodies in imperfectly cleaned slides; fragments of dirt, which the leucocytes rapidly take up, are apt to mislead.

According to Metschnikoff, the lymphocyte has no phagocytic action in malaria. This observation I believe to be correct. Several writers, however, have described and figured what they regard as malarial pigment in the lymphocyte. This, I am convinced, is founded on an error in interpretation and has arisen from ignorance of the fact that in all bloods, healthy and malarial alike, from 20 to 50 per cent. of the small mono-nucleated lymphocytes contain, lying in the narrow zone of cytoplasm, one or two minute round dots of intensely black material

optically indistinguishable from malarial melanin. I am not aware that this appearance has been described hitherto, but multiplied observation has convinced me of the accuracy of my statement. The discovery, therefore, of a speck of intensely black pigment in the lymphocytes must not be regarded as evidence of malarial infection.

Diagnosis of vacuoles.—The beginner may have a difficulty in determining whether certain appearances in the corpuscles are vacuoles, or whether they

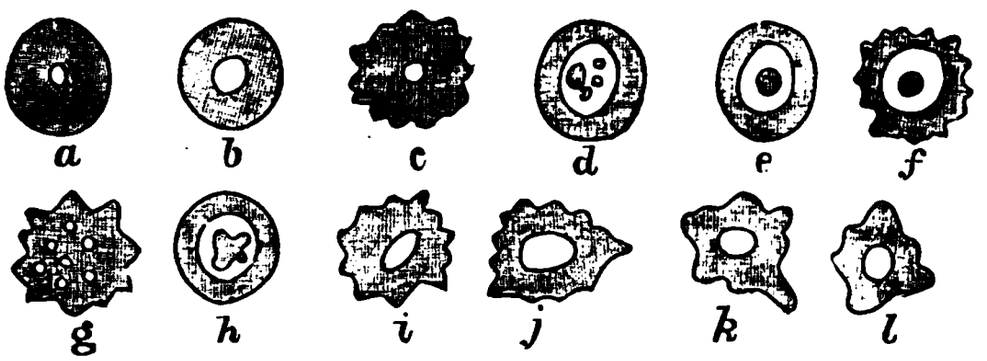

Fig. 12.—Vacuolated and crenated blood corpuscles. (*After Laveran and Blanchard.*)

a, *b*, *c*, blood corpuscles with central vacuoles, *c* is crenated; *d*, *e*, *f*, *h*, blood corpuscles with central vacuole, in the middle of which there is some fragmental hæmoglobin. Sometimes exceedingly minute egg-shaped vacuoles with a speck of hæmoglobin in the centre are met with, and are apt to be taken for parasites. *g*, crenated blood corpuscle with several small vacuoles; *i*, *j*, *k*, *l*, deformed blood corpuscles with central lacunæ.

are parasites. The following hints may help him to a correct decision. Vacuoles (Fig. 12, *a*, *b*, *c*, *d*, *e*, *f*, *h*, *i*, *j*, *k*, *l*) are very distinct, definite, clear, and have sharp edges; they have no amœboid movement, carry no pigment, and, of course, do not stain. Intracorpuscular plasmodia, on the contrary, are dim and, as a rule, ill-defined; they have soft, shaded-off edges; possess amœboid movements; when large, carry grains of pigment; and, of course, take the appropriate stains. It is hardly necessary to indicate the points of diagnosis from leucocytes or from cupped, folded, or crenated (Fig. 12, *c*, *f*, *g*, *i*, *j*, *k*, *l*) corpuscles.

Moribund and fragmented plasmodia.—Moribund—it may be fragmented—free parasites (Fig. 13) are often a source of confusion to the beginner. Their

nature is frequently misunderstood, they are sometimes erroneously termed "sterile bodies." They are, in fact, mechanically freed parasites expressed from blood corpuscles by the compression to which the blood is subjected between slip and cover glass. It must be borne in mind that the longer the blood is on the slide—particularly if evaporation be not prevented by vaseline ringing of the cover glass—the more closely will the cover-glass approximate to the slip, the greater

Fig. 13.—Free moribund plasmodia.

a b c, large swollen and fragmenting escaped parasites; *d, e, f*, the same vacuolating. (*Compiled from Thayer and Hewetson.*)

will be the pressure on, and consequent thinning and spreading out of, the blood corpuscles and parasites, and the greater the liability to damage of these very delicate bodies. Frequently the artificially freed parasites are broken into small fragments. The entire, as well as the fragmented, plasmodia on becoming free in the liquor sanguinis tend to assume a spherical or disc-like form; at the same time the protoplasm of which they are composed seems to become diffluent, and the pigment is resolved into a number of minute dust-like particles, possessing active, brownian movement. Some of these spherical or disc shaped bodies with dancing pigment particles are really crescent-derived spheres, belonging to what I regard as the mosquito cycle. These are parasites, which have escaped from corpuscles in a normal way, but which have become arrested in their evolution in consequence of the abnormal conditions in which they find themselves placed *in vitro*; others are the remains of flagellated bodies, the flagella having broken away.

The plasmodium as a means of diagnosis.—All of these multiform appearances the student must learn to recognise and interpret. Skill in this is merely a matter of time, practice, and reflection. Given these, the student should not only be able to diagnose by the microscope malarial infection, but he should also be able to recognise the type of any particular infection, the probable severity of the case, and the period of the fever cycle. For diagnosis in malaria, therefore, skill in the microscopic examination of the blood is of the utmost value, and no pains should be spared by the practitioner in malarious countries to acquire it. In acute untreated malaria the plasmodium may be detected practically in every case. Thus Thayer and Hewetson —excepting in two or three instances where the patient's blood was examined only during convalescence—in 616 cases found the plasmodium in every instance. The best Italian and German authorities are equally emphatic on this point. Personally, I can assert that since I became familiar with the subject I have never failed to find the parasite in any acute untreated malarial case I have had a proper opportunity of examining. Whenever in a case of acute disease, supposed to be malarial, I have failed to do so, the case has turned out to be of quite another nature.

Bearing of quinine on microscopical diagnosis.—It is of little use to examine the blood for the intra corporeal forms of the plasmodium after full doses of quinine have been taken; the drug rapidly brings about the disappearance of this phase of the parasite. The crescent or extra-corporeal phase, however, is not affected by drugs, and is readily found in suitable cases for days after the patient is cinchonised.

On staining malarial blood.—As a general rule, the beginner should work only with unstained preparations of fresh liquid blood. To the unpractised staining is full of pitfalls. In such circumstances it

must not be relied on for purposes of responsible diagnosis. For the study of the morphology of the plasmodium, however, staining is of real value; moreover, some such method must be employed should permanent preparations be desired. The English reader will find full details of a variety of methods in Mannaberg's (Sydenham Soc.) and in Thayer and Hewetson's monographs (Johns Hopkins Hospital Reports, Vol. V.); here only one or two of the many methods can be described.

The following method I strongly recommend as being easy, rapid, and reliable: Cleanse with alcohol a dozen or more slips, and place them side by side in a row near the patient. Prepare half a dozen strips (1½ by ¾ inch) of smooth, uncrinkled guttapercha tissue, or of thinnest tissue paper. Prick the patient's finger. When a minute droplet of blood has welled out, take one of the strips of guttapercha tissue or of tissue paper and apply it to the exuded blood so that it touches the drop about ⅓ inch from one end of the strip. Immediately lay the charged strip, blood surface downwards, on one of the slips, and, after waiting a second or two until it is seen that the blood has spread out, draw the strip of guttapercha or paper, holding it by the uncharged end, along the glass.* A very fine film of blood, with beautifully regular and suitably disposed corpuscles, may thus be secured. A number of slips can be charged in this way in a few minutes. After the blood has dried, whenever it is desired to stain it, either at once or at any future and more convenient time, it should be fixed by dropping on the slip a little alcohol. After five minutes the alcohol is dried off with filter paper, and then a drop or two of aqueous solution of borax- (5 per cent.) methylene blue (2 per cent.) is spread on the film. After thirty seconds the slide is

* Another excellent plan of preparing films of malarial blood has been described by Dr Neil Macleod. In this plan the blood is taken up in the edge of a strip of stout note-paper and is spread on slip or cover-glass by drawing the paper, held at an angle, along the face of the glass.

thoroughly washed in water, dried with filter paper and afterwards by gently warming it over the spirit lamp. Finally, zylol balsam and a cover-glass are applied. Fixing and staining may be deferred to suit convenience, the slip being duly labelled for purposes of identification. This method I find is much easier, cleaner, more rapid, and more convenient than the usual way of making and staining films on cover-glasses. Needless to say, minute attention to cleanliness is indispensable.

On examination with a twelfth immersion lens of slides prepared in this way, the nuclei of the white corpuscles are seen to be very deeply stained, the

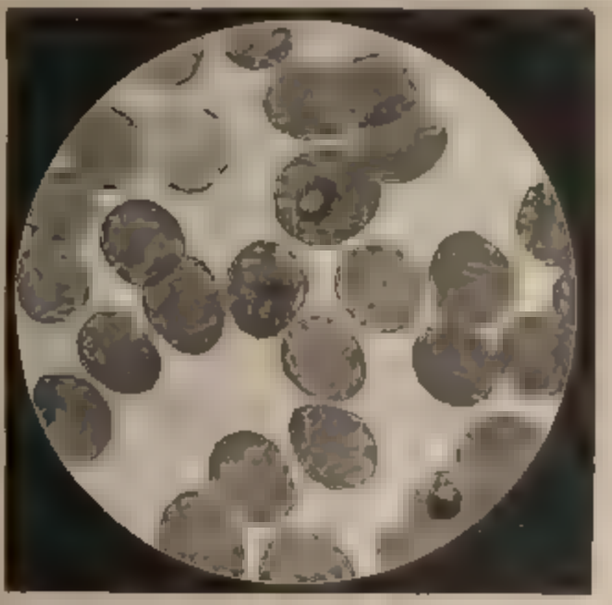

Fig. 14.—Young tertian parasite, stained with methylene blue. (× 1000.)

protoplasm of the white corpuscles is very lightly stained, whilst the parasites are stained an intermediate tint, and show up sharply enough in the faintly tinted red blood corpuscles (Figs 5, 11, 14, 15). Unless in practised hands, contrast staining with eosine is uncertain in its results in methylene blue preparations; even in these good preparations are the exception. For ordinary purposes I do not

recommend it, as it is superfluous and one can never be sure of the results.

Methylene blue preparations are apt to fade. By mounting the fixed film in iodine gum a more permanent preparation, in which the unstained parasite shows up well in the orange-coloured corpuscles, may be rapidly obtained. Ehrlich's acid hæmatoxylin five minutes, weak eosine half a minute, wash in tap water and then in distilled water, dry,

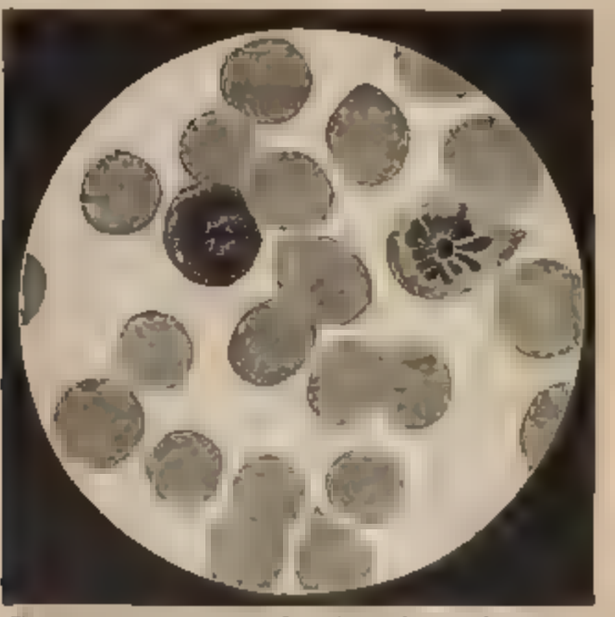

Fig. 15. [illegible] (× 1000.)

and mount in zylol balsam, is also an easily carried out and effective method for obtaining permanent preparations.

As already stated, staining is not so suitable for beginners as are fresh liquid preparations. There is one exception to this rule, however, and that is when crescents are to be sought for and there are but few of them present in the blood. In such circumstances the following method may lead to their detection when, owing to the small quantity of blood which can be efficiently searched in an ordinary liquid preparation, they might be overlooked or, at least, be very hard to find:

Spread with tissue paper, in the way already described, a *fairly thick* layer of blood on the slip. After this has dried, dip the slip in clean water for a second or two—not longer—so as to wash out the hæmoglobin. Fix immediately by pouring alcohol on the wet film. Dry, and then stain with borax-methylene blue, and mount in zylol balsam. It is better, though perhaps slightly more troublesome, first to fix the dried blood film with alcohol, then to dissolve out the hæmoglobin by a very short immersion in weak acetic acid (two drops to the watch-glassful of water); then wash away the acid, stain with methylene blue, wash, dry, and mount in zylol balsam. Owing to the large amount of blood that in such preparations can be rapidly scrutinised, to the absence of hæmoglobin, and to the very definite form of the objects sought for, if any crescents be present they are quickly detected even by a comparatively low power of the microscope—one-eighth or even one-sixth dry objective sufficing. The other forms of the plasmodium may also be detected by this method, but only by the practised eye.

Staining the flagellated body.—Thirty or forty strips (3 inches by 1½ inch) of thick blotting-paper, each having an oblong hole (1 inch by ⅔ inch) cut lengthways in its centre, are prepared; they are then slightly but sufficiently moistened with water and laid in rows on a sheet of window glass.

A patient, in whose blood the crescent form of the malaria parasite abounds, is selected. His finger is pricked, and a droplet of blood, the size of a large pin's head, is expressed. A clean microscope slip is then breathed on once, and the droplet of blood immediately taken up by lightly touching it with the centre of the breathed-on surface of the slip. The blood is now rapidly and somewhat unevenly spread out with the needle so as to cover an area of about ¾ inch by ½ inch. The slip is immediately inverted over a blotting-paper cell and pressed down sufficiently to secure thorough apposition

of the slip to the paper without, at the same time, bringing the blood into contact either with the moistened paper forming the wall, or with the glass forming the floor of what is now a very perfect moist chamber. The rest of the paper cells are rapidly covered with blood-charged slips prepared in the same way. In from a quarter to three-quarters of an hour the slips are removed and dried by gently warming them over the spirit lamp blood surface away from the flame. When dry, the films are fixed with absolute alcohol, a few drops being poured on each. After five minutes the alcohol is dried off, and a few drops of weak acetic acid (10 to 20 per cent.) are laid on the film and left there long enough thoroughly to dissolve out all the hæmoglobin. The slides are then washed in water and dried. They may now be stained with various reagents. So far, I have obtained the best results from weak carbol fuchsine (20 per cent.) and prolonged staining. The stain is dropped on the slip and covered with a watch-glass, after six to eight hours it is washed off, the slide dried, and a cover-glass applied with zylol balsam. The staining, though sufficiently intense, is fairly transparent.

Most of the slides will show numbers of spheres and several or many well-stained flagellated bodies (Figs. 3 and 4) Very few crescents remain untransformed. If the slips are removed and dried in from five to ten minutes after being placed on the blotting-paper cells, only crescents, ovals, and spheres will be found; if they are left for three-quarters of an hour to an hour, free flagella, and what Ross calls "spent pigment," may be found, the latter sometimes enclosed in phagocytes. Occasionally flagellated bodies are found partially included in phagocytes.

CHAPTER II.

CLASSIFICATION AND DESCRIPTION OF THE MALARIAL PARASITES AND THEIR ASSOCIATED FEVERS.

It may be asserted, in a general way, that the different clinical types of malarial disease are associated with different and corresponding types of plasmodia; but as to whether these different types of plasmodia are mere varieties, or whether from a zoological point of view they are distinct species, the evidence, so far, is insufficient to warrant a definite conclusion.

The point is by no means easily settled; nor is it likely to be decided until we are in possession of more information about the life-history of the organism outside the human body, and of such knowledge as will enable us to carry on sustained and continuous observations on individual parasites, and to institute experiments in cultivation and in inoculation with cultures.

Meanwhile, the varieties or possible species of plasmodia have been studied and classified according to:—

1. The duration of their respective life cycles inside the human body.
2. Their morphological characters.
3. The clinical phenomena they give rise to.
4. The results of inoculation experiments.

It may be said that, so far as these tests go, there is evidence either of plurality of species or of the existence of very stable varieties. That is to say, a particular clinical type of malarial disease is associated with a parasite of more or less definite morphological form and intra-corporeal life cycle,

characters which are maintained when the parasite has been inoculated experimentally.

In the treatment of this subject the classification suggested by Mannaberg will be followed, a classification based principally on the investigations of Golgi, Marchiafava, Bignami, Celli, and other Italians, as well as on his own most excellent work.

The forms of the malaria parasite and of the diseases they give rise to may be divided into two comprehensive groups—the benign and the malignant. A principal morphological distinction between these two groups is that, whereas the benign parasites never form crescent bodies, the malignant parasites form crescents. In the former the extra-corporeal flagellated phase is evolved from what appears to have been an ordinary intra-corpuscular plasmodium; in the latter the flagellated phase is evolved from crescent-derived spheres. A principal clinical difference between the two is that, whereas the benign parasite never gives rise to pernicious attacks, the malignant parasite may, and frequently does, give rise to such attacks. Herein lies an important practical diagnostic point, one which only the microscope can supply.

The benign parasites are of two kinds: One having a cycle of seventy-two hours, causing a fever recurring every three days—quartan ague; the other with a cycle of forty-eight hours, causing a fever recurring every two days—tertian ague.

The malignant parasite has at least three forms: A pigmented parasite of forty-eight hours' cycle; a pigmented parasite of approximately twenty-four hours' cycle; and an unpigmented parasite, also approximately of twenty-four hours' cycle.

We may arrange them thus:—

Benign	Quartan Tertian	Do not form crescents.
Malignant	Quotidian—pigmented Quotidian—unpigmented Tertian	Form crescents.

Formerly, classification being based entirely on clinical phenomena, malarial diseases were divided into quotidian, tertian and quartan intermittents or agues, and remittents; but since it has been found that what was designated remittent fever is produced both by quartan, tertian, and quotidian parasites—the fact of intermittency or remittency being more or less a matter of accident—it has been considered advisable to expunge the term remittent fever as indicative of a distinct species of plasmodium disease. Any one of the five kinds of parasites enumerated may cause what was known as remittent fever. The intermittency or remittency of any given fever depends, in great measure, on the simultaneousness or the reverse of the maturation of the crowd of parasites giving rise to it. If all the parasites present are of nearly the same age, they mature approximately simultaneously and we have an intermittent; if they are of different ages, they mature at different times scattered over the twenty-four hours and we have what was known as a remittent. Further, two generations of tertian parasites maturing on successive days will produce a quotidian fever, *tertiana duplex;* two generations of quartan parasites maturing on successive days will produce fever fits on two successive days followed by one day of freedom, *quartana duplex;* three generations of quartan parasites will produce what clinically appears to be a quotidian fever, but in reality is a *quartana triplex.*

The classification adopted must not be accepted as final; at best it is merely provisional. In actual practice it may be hard, often impossible, to bring the cases met with into exact line with such an arrangement. Moreover, it is necessary to bear in mind that this classification is based principally on observations made in a very limited district, principally in Italy, and principally on Roman fevers. It may not apply, therefore, to the entire malarial world. That it lies on a substratum of fact there can be no doubt; nor can there be much

doubt that it has in many particulars a general application to malarial disease as found all over the world. Still, judging from clinical facts, there seems ground for believing that there are other species or varieties of the plasmodium besides those described by the Italians, and that the list here given will have to be enlarged or recast in the future. Men with extensive experience of malarial disease in their own persons tell us that they can discriminate by their sensations and symptoms between the fevers of different localities. Analogy would incline us to believe that clinical differences of this sort depend on differences in the causal parasites How very different, for example, are the hæmoglobinuric fevers of Africa and the bilious remittents of India. Is it not probable that they depend on specifically distinct parasites or, at least, on more or less definite varieties?

CLINICAL PHENOMENA OF MALARIAL FEVER.

Before proceeding with a description of the various plasmodia and their associated fevers, there are certain generalities which, to save repetition, had better be mentioned here.

Intermittent fever or ague.—Every typical malarial fever is made up of a series of pyrexial attacks which recur at definite intervals of twenty four, forty-eight, or seventy-two hours. Each attack consists of a stage of rigor, a stage of heat, and a stage of sweating; these are followed by a period, "the interval," of apyrexia, actual or relative. The duration and intensity of the constituent stages vary considerably. On the whole, they observe a certain proportion to each other, the more pronounced the rigor, the higher the fever, and the more profuse the sweating. Such attacks, with well-marked intervals of apyrexia, are designated intermittent fevers or agues. The expression "ague" is by many applied only to intermittents having a pronounced rigor stage.

Premonitory stage.—Before rigor sets in, and sometimes for several days before the actual disease

declares itself, there may or there may not be a premonitory stage marked by lassitude, a desire to stretch the limbs and to yawn, aching of the bones, headache, anorexia, perhaps vomiting, perhaps a feeling as of cold water trickling down the back. If the thermometer be used at this stage, it will be found that body temperature begins to rise some two or three hours before the other and more striking symptoms which ensue set in.

Cold stage.—When rigor sets in the feeling of cold spreads all over the body, becoming so intense that the teeth chatter and the patient shivers and shakes from head to foot. He now seeks to cover himself with all the wraps he can lay hands on. Vomiting may become distressing. The features are pinched, the skin blue and cold-looking, the fingers shrivelled. The feeling of cold is entirely subjective; if the temperature be taken, it is found to be already several degrees above normal, and to be rapidly mounting. In young children it is not at all unusual to have a convulsive seizure at this stage; a fact that has to be borne in mind, as it is very apt to lead to ideas of epilepsy.

Hot stage.—After a time the shivering gradually abates, giving place to, or alternating with, waves of warmth and, before long, to persistent feelings of intense heat and febrile distress. The wraps, which before were so eagerly hugged, are now tossed off; the face becomes flushed; the pulse is rapid, full, and bounding; headache may be intense; vomiting frequent; respiration hurried; the skin dry and burning; the thermometer mounting to 104°, 105°, 106°, or even higher.

Sweating stage.—After one or more hours of acute distress, the patient breaks out into a profuse perspiration, the sweat literally running off him and saturating his clothes and bedding. With the appearance of diaphoresis the fever rapidly declines; headache, vomiting, thirst, and febrile distress giving place to a feeling of relief and tranquillity. By

the time the sweating has ceased the patient may feel quite well; a little languid, perhaps, but able to go about his usual occupation. The bodily temperature is now often sub-normal, and may remain so until the approach of the next fit one, two, or three days later.

Duration of the fit.—The duration of an ague fit and of its constituent stages is very variable. On an average it may be put at six to ten hours; the cold stage occupying about an hour, the hot stage from three to four hours, the sweating stage from two to four hours.

The urine in ague.—During the cold stage the urine is often limpid and abundant, and is passed frequently; but during the hot and sweating stages it is scanty, loaded, sometimes albuminous. The amount of urea is increased, particularly during the cold stage, and so are the chlorides. The phosphates, on the contrary, diminished during the rigor and hot stages, are increased during defervescence. The augmentation in the excretion of urea commences several hours before the subjective symptoms of the attack begin, attains its maximum towards the end of rigor, and decreases during the hot and sweating stages although still continuing above the normal standard. The excretion of carbonic acid follows a corresponding course. Dr. Sydney Ringer was the first to point out the interesting fact that, although the return of fever may be prevented by the administration of quinine, yet, for a time, a periodic increase in the excretion of urea occurs on the days on which the fever fit was due. The urine is often deeply coloured, giving with nitric acid the play of colour characteristic of bile pigment, or the brown colour described by Gübler as "hæmapheic." Glycosuria does occur, but is by no means common.

The spleen during the fit.—The spleen becomes enlarged to a greater or less extent during rigor. The swelling disappears at first in the interval, but tends to become more or less of a chronic feature if

the attacks recur frequently, more especially if they are associated with pronounced cachexia.

Period of the day at which ague commences.—Two-thirds of agues come off between midnight and midday. This is an important fact to remember in diagnosis; especially when we have to face the possibility of recurrent pyrexial attacks being dependent on such conditions as liver abscess, tuberculosis, and septic states—conditions, be it remarked, in which febrile recurrence takes place almost invariably during the afternoon or evening.

Atypical agues.—Such is a brief sketch of the leading features of a classical ague fit. Cases, however, are frequently met with in which all of these symptoms are very much toned down; in which, perhaps, a periodically recurring feeling of coldness followed by languor, or a slight headache, or a slight rise of temperature, are the only symptoms indicating the presence of the malaria parasite in the blood. In some fevers, and these by no means the least dangerous, the subjective symptoms may at first be of so mild a character that the patient is able to go about his duties with a body temperature of 103° or 104°; he may have no severe rigor, no headache, no severe gastric symptoms, no acute febrile distress of a disabling character. Some of the African fevers—so liable to assume suddenly a pernicious character—are of this nature. On the other hand, notwithstanding a comparatively slight rise of temperature, headache, languor, vomiting, may be extremely distressing. There is an infinite variety in this respect. Evidently the toxin of the plasmodium is far from being a simple body; probably, like turberculin, it contains several ingredients arranged in different proportions in the several varieties of the parasite. Doubtless, also, the degree of infection, various combinations of the varieties of plasmodia, and individual idiosyncrasy play a part in determining the intensity and character of the reaction of the body to the toxins created by the plasmodium.

Terms employed. Acute malarial attacks which recur daily are called *quotidian ague*: if they recur every second day they are called *tertian ague*; if every third day, they are called *quartan ague*. As a rule, the attacks tend to occur about the same time every day In some cases the time of recurrence becomes earlier each day; such fevers are said to *anticipate*. Or they may occur at a later hour, in which case they are said to *postpone* When the attacks are prolonged, so that one attack has not concluded before the next commences, the fever fits are then said to be *subintrant* When the fit is prolonged and periodicity is marked by only a slight fall of temperature, a slight sweating, a slight feeling of chilliness, the fever is said to *remit* to be a *remittent* Sometimes there is no remission; such a fever is called *continued*. It occasionally happens that two distinct pyrexial attacks come off on the same day; such a fever is said to be *double*. All sorts of blendings of quotidians, tertians, and quartans occur, in such the infection is said to be a *mixed infection*.

Relation of the phenomena of the fever fit to the stages of the parasite. All these differences and peculiarities in the clinical phenomena of a malarial attack, as indicated by the foregoing terms, complicated and hard to interpret in many cases though they be, are, it is believed, directly correlated to the phases of the intra-corporeal life of the plasmodium, this organism is, in fact, the key to their interpretation. As already mentioned, as the time of rigor approaches the pigment of the parasite, hitherto scattered throughout the substance of the little animal, becomes concentrated, and the sporulating body develops. Shortly before and during rigor, and as a direct cause of rigor, these sporulating bodies are breaking up and, presumably, liberating their toxins. At the end of rigor, during the hot, and during the sweating stages, the young parasites of the new generation, the small intra-corpuscular bodies, and the

leucocytes carrying the pigment liberated at the breaking up of the sporulating bodies are in evidence, and the toxins liberated at the same time are being eliminated. During the interval the intra-corpuscular parasites grow, become pigmented, and prepare for maturation. From the fact that parasites are present in the blood during apyrexia, and often in great abundance, it is evident that it is not the mere presence of the parasite in the blood corpuscles that causes the fever; most likely the pyrogenic agency is some toxin which is liberated when the sporulating parasite breaks up and becomes free in the liquor sanguinis. Consequently, we find that in remittent and continued types of malarial fevers sporulating plasmodia may be met with at all stages of the fever; and, conversely, that when plasmodia are met with at all stages of development the associated fever is probably remittent or more or less continued in type.

The foregoing are generalities which apply to all the types of malarial fever.

BENIGN QUARTAN INFECTION.

The parasite.—The parasite of quartan fever (Plate I., Fig. 1) has a cycle of seventy-two hours. At its earliest stages of epi-corpuscular and of early unpigmented intra-corpuscular life it takes the form of a small, roundish, clear speck (Plate I., Fig. 1, *a*), showing up somewhat distinctly against the hæmoglobin of the invaded corpuscle. At this stage, as contrasted with the other varieties of plasmodia, it is further distinguished by the feebleness of its amœboid movement. Later, as soon as it becomes pigmented (Plate I., Fig. 1, *b*, *c*, *d*, *e*, *f*), all amœboid movement ceases. Relatively to the other plasmodia, the pigment carried by the quartan is large in amount and coarse in grain, sometimes forming short rods. The sporulating body (Plate I., Fig. 1, *g*, *h*), is made up of eight to ten elements arranged daisy fashion and, usually, very symmetrically around the now centrally placed and massive block of very black pigment. About the

centre in each of the spherical or pear-shaped spores, which are slightly rough in outline, a shining nucleolus can usually be readily made out. The quartan parasite, never forming crescents, derives its rarely seen flagellated form from what looks like an ordinary large intra-corpuscular pigmented parasite (Plate I., Fig. 1, *i*) that has escaped from the red corpuscle in which it has developed. This phase, rarely seen, occurs almost exclusively during the pyrexial stage of the cycle. Further, the quartan parasite does not, as does that next to be described—the tertian parasite, cause marked hypertrophy of the blood corpuscle in which it lies. When mature it completely fills the normal-sized corpuscle, scarcely a rim of hæmoglobin being visible (Plate I., Fig. 1, *e*); so that it sometimes looks at this stage as if it were a free and independent body floating about in the liquor sanguinis. All quartan parasites do not proceed to spore formation or flagellation; some are said to degenerate into peculiar clear, dropsical-looking spheres filled with dancing particles (Plate I., Fig. 1, *i*), which form a striking feature in certain malarial bloods. A considerable proportion of these free, dropsical-looking bodies are probably parasites which, after being placed on the microscope slide, and after escaping from corpuscles, have failed to project flagella. This failure to exflagellate is probably not normal, but an effect of mechanical disturbance from pressure of the cover-glass, or of other circumstance inherent in the artificial conditions under which we necessarily observe these bodies. In more normal conditions, as in the mosquito, exflagellation may be more frequently effected.

The "daisy"—as it is sometimes called—or sporulating form of the quartan parasite is more frequently seen in the peripheral blood than is the corresponding phase of the other malarial parasites. For this reason, and because of the easy visibility of the parasite at all its stages, owing to its size and to the large amount of pigment it carries, and because the entire intra-corporeal cycle is completed in the peripheral

blood, the quartan is the best form of plasmodium for the beginner to study.

Geographical distribution.—The fever which the quartan parasite gives rise to—single, double, or

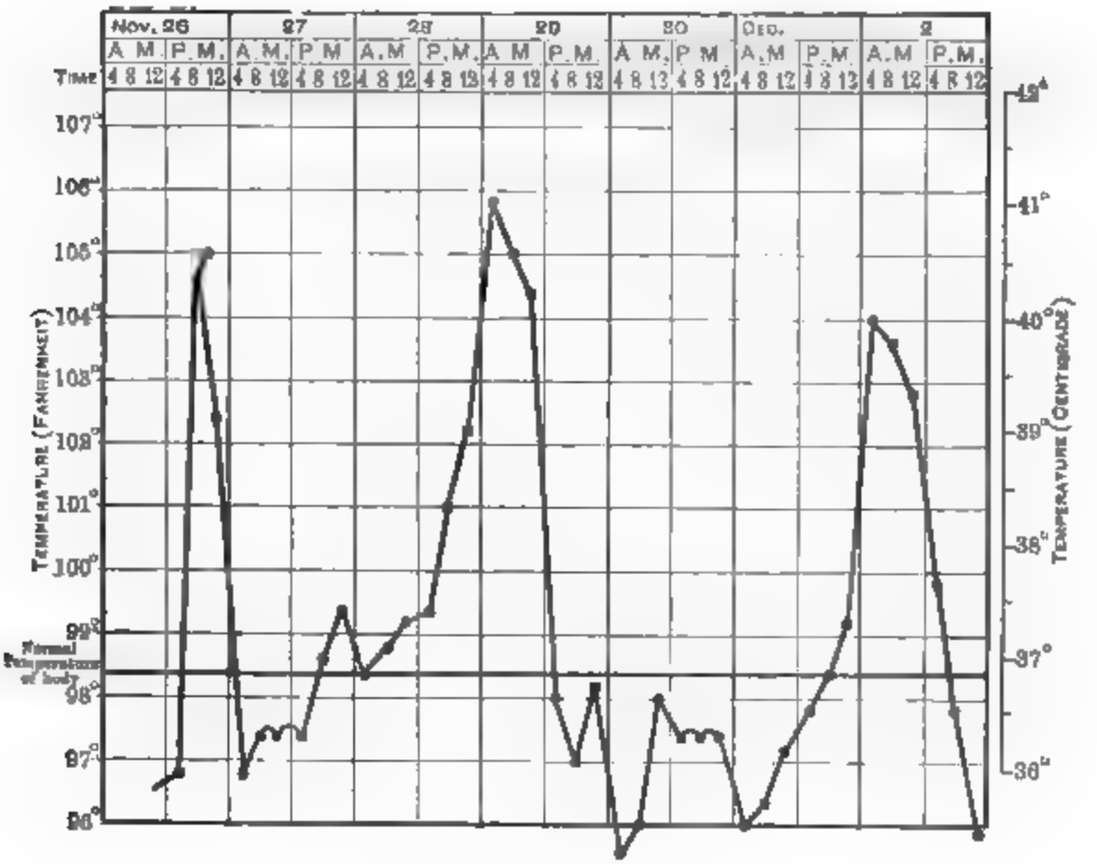

Fig. 16.—Chart of quartan ague.

treble quartan ague—is, relatively, much more common in temperate latitudes than in the tropics. Formerly it was common enough in England, and is still far from rare in the malarious districts of north and mid-Europe, and, doubtless, elsewhere in similar climatic and telluric conditions. But, as we proceed south, it becomes, relatively to the other forms of malaria, rarer, until in the tropics in some places it almost disappears. Thus in a paper read at the Calcutta Medical Congress of 1894, Dr. Crombie mentions that in his large experience he rarely sees quartan ague.

As his experience applies particularly to Calcutta and its environs, it may not hold for the whole of India; in fact, Ross (*Ind. Med. Gaz.*, Feb. 1896) and others state that the quartan parasite is common enough in Madras and elsewhere in India. The general statement, however, that quartan ague is more a disease of the temperate zones than of the tropics, probably expresses the truth.

The associated fever. The ague fit in quartan is generally smart while it lasts, and well defined as regards its constituent stages (Fig. 16). It does not tend so markedly, as is the case with the other malarial infections, to the rapid development of cachexia.

BENIGN TERTIAN INFECTION (SPRING TERTIAN OF THE ITALIANS).

The parasite.—The early stage of the benign tertian parasite (Plate I., Fig. 2) resembles that of the quartan inasmuch as it consists of a small pale speck on, or in, the invaded red blood corpuscle (Plate I., Fig. 2, *a*); it differs in exhibiting very much greater amœboid activity, changing its form incessantly, besides pushing out and retracting pseudopodia (Plate I., Fig 2, *b*) This amœboid activity persists during growth and the acquisition of pigment, though in a progressively diminishing degree; it gives rise to great and rapidly changing irregularities in the contour of the parasite (Plate I., Fig. 2, *c*, *d*, *e*). It is almost entirely suspended by the time pigment concentration is effected. In the tertian parasite the pigment particles are, on the whole, finer than in the quartan parasite; and, moreover, are in a state of much more active and incessant movement, constantly changing their position in the peripheral layer the ectosarc of the amœba-like parasite—in which they, for the most part, lie (Plate I., Fig 2, *f*). Another, and markedly characteristic, accompaniment of tertian parasite infection is the considerable hypertrophy and marked decolorisation of many of

the corpuscles containing the organism (Plate I., Fig. 2, *d*, *e*, *f*, *g*). Sometimes the affected corpuscles seem nearly twice the diameter of the healthy ones; and nearly always, if the plasmodium is of any magnitude, the rim of hæmoglobin surrounding the parasite

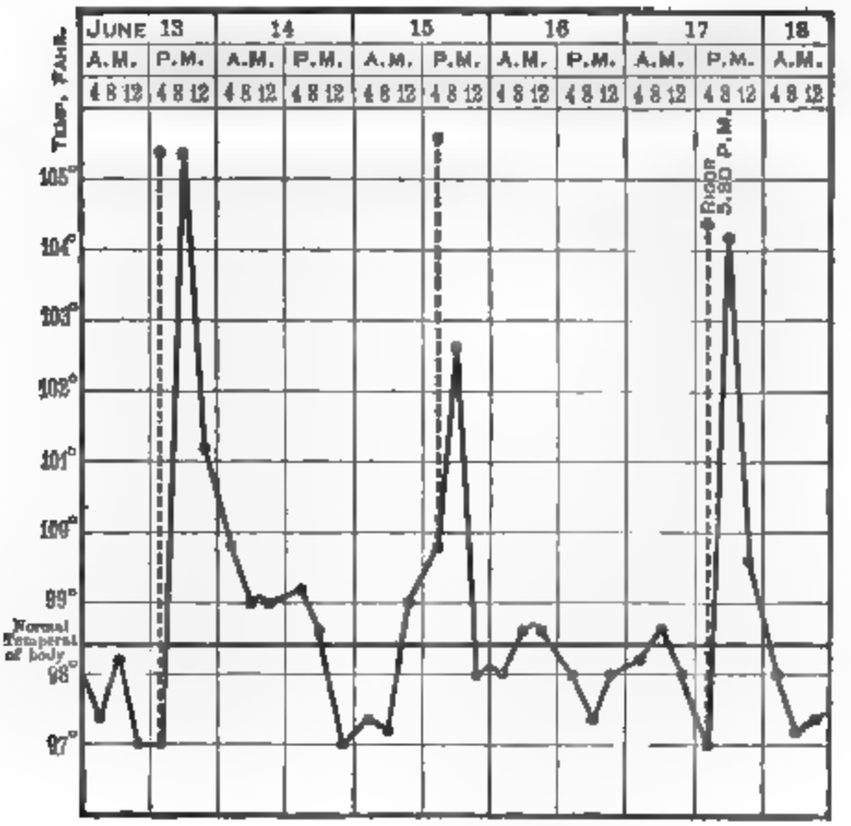

Fig. 17.—Chart of benign tertian ague.

has a "washed-out" look, sometimes being almost colourless.

In the tertian parasite when segmentation is completed the resulting body, instead of the very symmetrical, daisy-like figure of the quartan sporulating body, resembles rather a cluster of grapes in some more or less central part of which one or two masses of black pigment have accumulated among the berries (Plate I., Fig. 2, *h*; also, Figs. 1 and 2, *b*). The little spores forming the cluster—fifteen to twenty in number

—are smaller, smoother, and more spherical than those of the quartan parasite, seldom, in the unstained condition, exhibiting their nucleoli. I believe that in natural, uncompressed conditions the tertian rosette tends to pass from the disc form, impressed on it originally by the shape of the corpuscle, to something more approaching a globular form.

In benign tertian the flagellated body is formed in the same way as in the quartan parasite—that is, from an escaped intra-corpuscular pigmented body (Plate I., Fig. 2, *j*). It is seen particularly, just as in the case of the quartan infection, and not infrequently about the time of rigor.

Geographical distribution. — The benign tertian parasite, probably the commonest form of plasmodium, occurs in temperate and tropical latitudes alike. It is often found as a double infection and is, perhaps, the most frequent cause of quotidian as well as of tertian agues.

The associated fever.—The fever it gives rise to, except in the matter of the spacing, which is one of forty-eight hours, resembles that caused by the quartan parasite (Fig. 17).

MALIGNANT INFECTIONS (ÆSTIVO-AUTUMNAL OF THE ITALIANS).

The three parasites (Plate I., Fig. 3, and Plate II., Fig. 1) described by the Italian pathologists in connection with malignant malarial infection, although often associated together as well as with the benign parasites, are each of them occasionally found in what might be termed a pure culture. From a study of such cases the morphological and distinguishing characters of the different species, and their special pathological effects, have been more or less satisfactorily made out. Although much remains to be done, enough is already known to enable us, in a measure, to differentiate the parasites from each other as well as from the benign plasmodia, and to justify their being placed in a group by themselves.

FIG. 1.

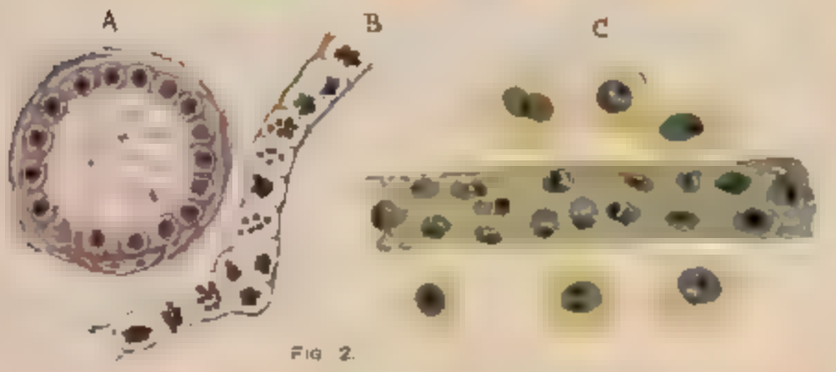

FIG. 2.

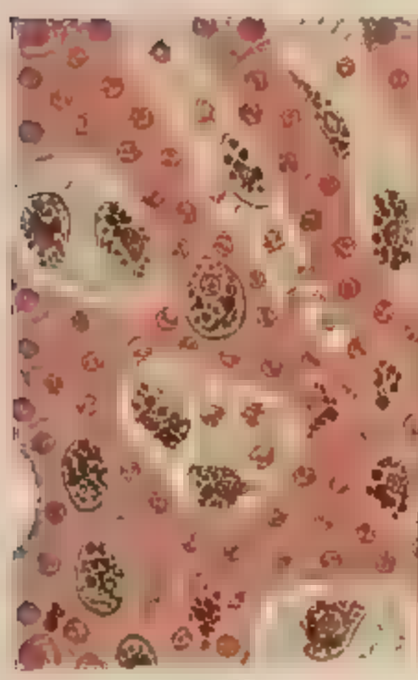

FIG. 3

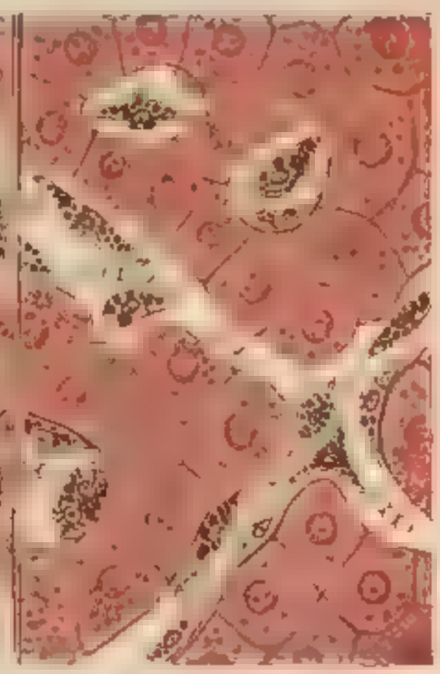

FIG. 4

PLATE II

Fig. 1. Parasites of the pigmented malignant quotidian (*Marchiafava and Bignami*). **Fig. 2.** Brain capillaries containing malaria parasites. A transverse section of the blood corpuscles at periphery invaded by unpigmented parasites. B vessel filled with sporulating unpigmented parasites, blood corpuscles in capillary and others free in the brain substance, each containing small pigmented parasites (*Mannaberg*). **Fig. 3.** Pernicious malaria (spleen). **Fig. 4.** Pernicious malaria (liver) (*Kelsch and Kiener*).

Characters possessed in common by the malignant parasites.—One notable feature in regard to them is that they are very much smaller than the benign parasites. The earlier unpigmented phase, owing partly to minuteness, partly to its forming but a thin and very transparent amœba in the hæmoglobin, is hard to see. When first mounted on the slide the amœboid movements are very active (Plate I., Fig. 3, *d*). In a short time this subsides somewhat, and then the little parasites tend to assume a more passive condition and to arrange themselves as tiny, though very definite and easily recognised, rather bright, colourless rings (Plate I., Fig. 3, *a*, *b*, *c*, *e*). Sometimes these rings may revert to the amœboid condition, and this perhaps for several times in succession; ultimately the ring form becomes permanent. Multiple infection of individual corpuscles (Plate I., Fig. 3, *g*) is often encountered, and this much more frequently than in the benign infections; doubtless this is owing to the prodigious number of parasites which, in these infections, are sometimes present in the circulation. As development advances the plasmodium-infected corpuscles seem to be filtered out by the capillaries and small arteries (Plate II., Fig. 2, A, B, C) of the deeper viscera and of the bone marrow; so that even in severe infections the pigmented stage is by no means proportionately represented by, or even frequently encountered in, finger blood, the sporulating stage (Plate I., Fig. 3, *i*, *j*) still less so. To find numerous examples of the more advanced stages of these parasites it is necessary to aspirate splenic blood, or to search in fatal cases in the deeper viscera, or in the bone marrow immediately after death. Owing to the absence of the more advanced forms from the peripheral circulation, the duration of the life span of these parasites is difficult to fix; probably it varies between twenty-four and forty-eight hours, being not very constant even in the same types.

"*Brassy bodies.*"—The malignant parasite frequently leads to a peculiar shrivelling of the invaded

corpuscle, resulting in the formation of a crenated, or folded, very dark corpuscle. This dark, irregularly-shaped corpuscle the Italians, from its colour, have designated "brassy body" (Plate I., Fig. 3, *e*). In the interior of these dark, shrivelled corpuscles the parasite can generally be made out as a minute, pale ring.

The crescent body characteristic. -Most distinctive feature of all, the malignant parasites alone form crescent bodies.

Time when crescents appear; not a fever form. – It is to be remarked that these crescent bodies are not to be seen at the very commencement of an infection. A week usually elapses between the first appearance in the peripheral blood of the small, intracorpuscular plasmodia and the first appearance of the crescent bodies. Once the latter begin to appear they generally tend to increase in number during a few days. They may persist, though, after a time, in decreasing numbers, in the circulation for one, two, or three weeks after the small, fever-causing, intracorpuscular plasmodia and their associated fever have disappeared, whether spontaneously or in consequence of the administration of quinine. Although when given early in an infection quinine may prevent the appearance of crescents, yet, once formed, this drug has apparently no influence on these bodies nor on their capacity for exflagellation The crescent body does not cause fever; it is usually associated, however, with marked cachexia.

Characters of the fever.—It is found that the fevers these parasites give rise to are apt to be very irregular in their course. The rigor stage is relatively less marked, the pyrexial stage is more prolonged, and is often characterised by a tendency to adynamic conditions, vomiting, intestinal catarrh, pains in the limbs, anorexia, severe headache, depression After apparent recovery from the fever, there is a great proneness to relapse at more or less definite intervals of from eight to fourteen days. Such fevers are accompanied by rapid destruction of corpuscles,

and are usually followed by marked cachexia. At any time in their course pernicious symptoms of the gravest character may declare themselves.

MALIGNANT QUOTIDIAN INFECTIONS.

The parasite.—The parasite of these infections is of two kinds, very generally in association —the pigmented (Plate II., Fig. 1) and the unpigmented. In both the cycle is approximately one

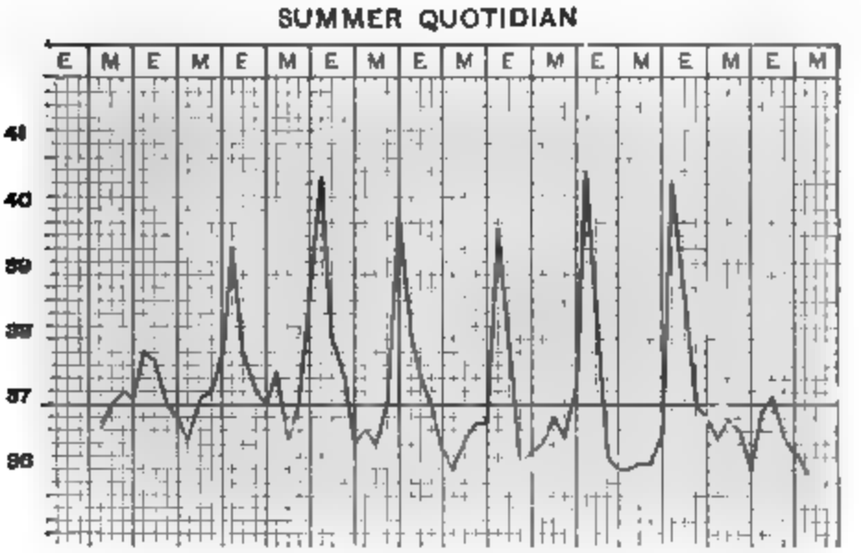

Fig. 18.—Chart of malignant quotidian infection.

of twenty-four hours; in both the young parasites exhibit very active movements, and tend to assume the ring form. Before sporulation, they grow so as to occupy from one-fifth to one-third only of the corpuscle. Both form little heaps of from six to eight very minute spores.

In the unpigmented parasite pigment is never seen unless in the crescent phase; in this phase, however, pigment is never absent. In the pigmented parasite there is a considerable amount of fine pigment which, at the sporulating stage rarely seen in peripheral blood, collects in the usual way into one or two more or less central lumps.

Character of the fevers.—The fever these parasites give rise to is such as just described, a typhoid-like depression being generally a prominent feature in well marked cases (Fig. 17).

MALIGNANT TERTIAN INFECTION.

The parasite.—The parasite (Plate I., Fig. 3) of this infection is, in many respects, like that of ordinary benign tertian, only smaller, attaining when mature from a half to two-thirds the size of the corpuscle it occupies. The infested blood-corpuscle may be altered in colour in the direction of being either darker or lighter; sometimes it shrinks, or it may become a "brassy body." The segments of the rarely encountered mature parasite number usually ten or twelve, and are arranged along with the associated clump or clumps of pigment in an irregular heap. The crescent is also, of course, a distinguishing feature of the infection.

The associated fever.—The symptoms this parasite gives rise to are, in many respects, very different from those caused by the benign tertian parasite. In the first place, though rigor is not so marked, the hot stage lasts longer often exceeding twenty-four hours; in fact, the tendency for the successive paroxysms to overlap, to become subintrant, is very marked. Moreover, where the intermissions are distinct, Marchiafava and Bignami have pointed out that the crisis is unlike that of ordinary tertian. There is what is called a double crisis; that is to say, when the fever has attained its apparent fastigium there is a drop of one or more degrees of temperature the "false crisis," to be followed by a fresh rise, which is then followed by the true crisis. This peculiar phenomenon the writers referred to attribute to the presence of two swarms of parasites, one of which matures somewhat later than the other (Fig. 18).

The tendency to the development of pernicious symptoms, to the production of cachexia, and to

relapse is similar to what occurs in the case of the malignant quotidian infections.

Geographical distribution.—All these malignant parasites are confined to the warmer regions of the earth, and to the more intensely malarial districts in these. In the sub-tropical zones they

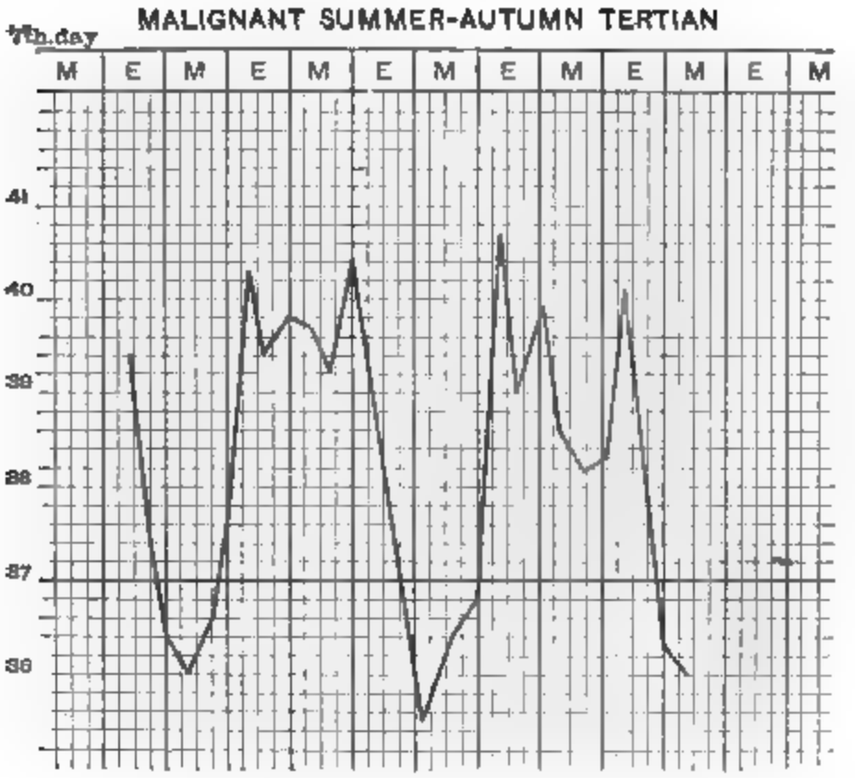

Fig. 19. Chart of malignant summer-autumn tertian.

occur as first infections only in late summer or early autumn; hence the name "æstivo autumnal."

Microscopical examinations in malignant fevers. It is important to bear in mind that in malignant infections the pigmented fever-causing forms of the parasite are not very frequently met with in peripheral blood. When found, and when it is observed that the pigment has become concentrated, it is a sure indication that a paroxysm is impending. On the occurrence of rigor, and at least during the earlier stages of the paroxysm, many small unpigmented

plasmodia, sometimes exhibiting active amœboid movement, sometimes appearing as rings, will be found in finger blood, but towards the end of fever these unpigmented plasmodia often diminish in number, and all evidence of parasitic infection may even disappear from the blood till the approach or incidence of the next paroxysm. Crescents and pigmented leucocytes may be numerous in the intervals of absence of the intra-corpuscular parasites. The segmenting forms of the malignant parasite are best found by aspirating the spleen with a hypodermic needle hardly a justifiable procedure unless in very exceptional circumstances; only very occasionally are they encountered in peripheral blood.

CLINICAL FORMS OF BENIGN AND PERNICIOUS MALARIAL FEVERS.

General statements. The foregoing account, so far as it goes, and so far as it relates to the clinical manifestations produced by uncomplicated and typical infections, is true enough. It must be borne in mind, however, that as there may be an infinite variety as regards the dosage of the parasite, and as regards individual susceptibility, and as there may be a concurrence of several species of plasmodia (mixed infection being far from uncommon), or of several generations of the same species of plasmodium maturing at different times, so there may be corresponding infinite variety in the clinical manifestations. Certain general statements may be made about them, however.

In more temperate climates, and in the winter and spring seasons of warmer latitudes, malarial fevers are usually distinct intermittents; and fresh infections occurring in these places and seasons, so far as the subject has been studied, are found to be produced by the benign tertian and quartan parasites, and are, therefore, of little danger. Relapses, however, of previous malignant crescent-forming parasite infections, originally contracted during the hot

weather, may occur during the cold season; in fact, they are far from uncommon.

First attacks, though produced by one of the benign parasites, may assume the characters of a remittent; generally, in temperate latitudes, they are frank intermittents. First attacks of malignant malaria, although they may in a few instances be intermittent, are in the majority of cases remittent in type; and so are attacks the result of extensive reinforcement by fresh parasites (through fresh exposure) of the old stock which the old fever subject may carry about him in a latent condition. The first attack experienced by a newcomer to a highly malarious district with a hot climate is, therefore, generally remittent and severe.

It is neither necessary nor desirable to attempt to describe in detail the infinite variety malarial attacks assume. It would be impossible in a limited space to do so; and, if done, the result would amount only to an uninteresting and unprofitable ringing of the changes on rigor, pyrexia, diaphoresis, bilious vomiting, bilious diarrhœa, constipation, catarrhal gastritis, headache, bone-ache, prostration, and so forth. The picture would be further confused by the fact that the natural procession of events is generally, nowadays, broken in on by the action of quinine, the use of which is almost universal with Europeans in the tropics; so that it is difficult to say how any given malarial fever would develop, or how it would terminate, if left alone. Sometimes, in the case of natives of tropical countries, who may not always command a few grains of quinine, such fevers pass into a typhoid state, with dry brown tongue, sordes in the mouth, muttering delirium, and may terminate in collapse and death. In others, untreated remittents and intermittents gradually subside spontaneously in the course of a week or fortnight; or the remittent may merge into an intermittent, which, in the course of weeks or months, subsides for a time, to recur every now and again at longer or shorter intervals. The Italians describe a form of malarial

fever the natural evolution of which seems to be in intervals of several days' or weeks' duration "long interval fevers," they call them. In these the fever seems to subside spontaneously. Kelsch and Kiener allowed certain cases of remittent to run their course unchecked by quinine; they found that in ten or twelve days the fever gradually expended itself Under favourable hygienic conditions the plasmodium and the associated fever frequently disappear together spontaneously.

REMITTENT TYPES.

Bilious remittent. One type of fever, known as bilious remittent, has long been recognised on account of the bilious vomiting, gastric distress, sometimes bilious diarrhœa, sometimes constipation, which accompany the recurring exacerbations. It is further distinguished by the pronounced icteric or, rather, reddish yellow or saffron tint of skin and scleræ; a tint derived, probably, not from absorption of bile as in obstructive jaundice but from modified hæmoglobin (hæmapheine) free in the blood or deposited in the derma. These bilious remittents are very common in the more highly malarious districts of Africa, America, the West Indies, India and, in fact, in all tropical countries. They are not specially nor directly dangerous in themselves, but they result usually in profound anæmia, and are often but the prelude to chronic malarial saturation, bad health and invaliding.

Typhoid remittent. — A modification of the bilious remittent — what Kelsch and Kiener call "typhoid remittent"—is very much more grave as affecting life than the simple bilious remittent. In the typhoid remittent, typhoid symptoms—such as low delirium, prostration, dry tongue, swelling of spleen and liver, subsultus tendinum, marked melanæmia—are superadded to the usual symptoms. Though recovery is the rule, a considerable proportion of such attacks prove fatal.

Adynamic remittent.—The same writers class

by themselves a set of cases they call "adynamic remittent"; cases which are characterised by fatuousness, restlessness, nervous depression, intense muscular and cardiac debility, profound and rapid blood deterioration, icterus, leucocytosis, melanæmia, liability to syncope, occasionally hæmoglobinuria, liability to hæmorrhages, and a marked tendency to local gangrene.

PERNICIOUS ATTACKS.

Many writers have drawn attention to what are called pernicious attacks or pernicious symptoms—the French neatly designate them "accès pernicieux"—a series of phenomena, the possibility of the appearance of which, not only in the course of remittents but in the course of what is seemingly only an ordinary paroxysm of intermittent fever, should never be lost sight of by the practitioner in tropical climates. These "accès pernicieux" may supervene in apparently mild cases, and carry off the patient with horrifying suddenness—as suddenly as an attack of malignant cholera. The wary practitioner is always on the look-out for them, and is always prepared with measures to meet them promptly when they threaten.

Pernicious attacks are roughly classified into cerebral and algide. The cerebral are divisible into hyperpyrexial, comatose, convulsive, paralytic, and so forth; the algide into syncopal, choleriform, dysenteric, hæmoglobinuric, etc.

Cerebral Forms.

Hyperpyrexial.—There can be little doubt that many of the cases of sudden death from hyperpyrexia and coma, usually credited to what has been called "ardent fever" or to "heat apoplexy," are really malarial. If careful inquiry be made into the antecedents of many of these cases a history of mild intermittent will often be elicited; or it will be found that the patient had been living in some highly malarious locality.

In the course of what seemed to be an ordinary malarial attack, temperature, instead of stopping at 104° or 105° Fahr. may continue to rise, and passing 107°, rapidly mount to 110° or even to 112°. The patient, after a brief stage of wild maniacal, or, perhaps, muttering delirium, becomes rapidly unconscious, then comatose, and dies within a few hours, or perhaps within an hour, of the onset of the pernicious symptoms.

Comatose. Or the patient, without hyperpyrexia, the thermometer perhaps not rising above 104°, may lapse into coma. The coma may pass away with crisis of sweating; on the other hand, an asthenic condition may set in, and death from collapse supervene.

Other cerebral forms.—In addition to these hyperpyretic and comatose conditions, other forms of cerebral attack are met with in the course of malarial fevers, such as *sudden delirium* ending in coma and, perhaps, death; *convulsive seizures* of an epileptic or of a tetanic character, with or without delirium or coma, which seizures, if not fatal, may eventuate in *permanent psychical disturbances*; various *forms of apoplectic like* conditions, and *paralysis* which may be complicated with *aphasia*.

Embolism of cerebral capillaries.—These cerebral attacks are now explained, and, it appears to me, correctly explained, by the supposition, founded on actual *post mortem* observation, that they depend on embolism by the malaria parasite of the capillaries of the various nerve centres (Plate II., Fig. 2) involved; in hyperpyrexia, the thermic centres, in aphasia, Broca's convolution; and so on. By microscopical examination of properly prepared sections of the brain in fatal cases, such a plugging of the vessels can generally be readily observed. The earlier students of malarial melanæmia had remarked the presence of pigment in the cerebral capillaries in many cases of this description, and attributed the associated symptoms to thrombosis by the pigment. Frerichs,

having failed to find pigment in certain fatal malarial cases attended with cerebral symptoms, whilst he found it in abundance in others in which there had been no special cerebral manifestations, rejected this hypothesis. At that time the malaria parasite had not been discovered, and Frerichs was not aware, of course, that there is a variety of the malaria parasite which does not form pigment; nor were the facts of localisation of the cerebral functions so well understood then as they are at the present day.

Malarial amaurosis.—In rare instances the patient may come out of the comatose condition of a pernicious malarial attack quite blind. The amaurosis is usually very transient, lasting for an hour or two only. On the other hand, it may be persistent; in which case, according to Poncet, optic neuritis, peripapillary œdema, extravasation of leucocytes, plugging of retinal and choroidal vessels by parasites or pigmented leucocytes and consequent multiple hæmorrhages, may be found in the fundus. If the hæmorrhages are minute they are discoverable by the microscope only. These fundus changes differ from those in quinine amaurosis. In the latter the amaurosis is more persistent; the disc is white and the vessels are shrunken; there are no inflammatory symptoms, and central vision is the first to recover.

Algide forms.

The algide forms of pernicious attack, as indicated by the name, are characterised by collapse and extreme coldness of the surface of the body, and a tendency to fatal syncope. These symptoms usually coexist with elevated axillary and rectal temperature.

Gastric form.—This condition may be associated with, and in a measure dependent on, acute catarrhal dyspeptic trouble. It is accompanied by severe epigastric distress, tender retracted abdomen and incessant vomiting.

Choleraic form.—Malarial attacks are sometimes accompanied by choleraic symptoms. The stools

suddenly become loose, profuse and numerous; though not so profuse or colourless as the rice-water discharge which pours from the patient in true cholera. Generally they retain a certain amount of biliary colouring and may be mucoid or even bloody. As in cholera, the serous drain may lead to cramps in the limbs, loss of voice, pinched features, washer-woman's fingers, almost complete suppression of urine and, perhaps, to fatal collapse. Such attacks are very deceptive, and may be mistaken for true cholera. The high axillary temperature if present, a history perhaps of recent ague fits, the subsequent rapid disappearance of the choleraic symptoms on the appearance of the hot and sweating stages, the colour of the stools and other collateral circumstances usually suffice for diagnosis; particularly if they are supplemented by a microscopical examination of the blood. Although not usual, recurrence of the choleraic symptoms may take place at the next fever period. A dangerous type of malarial fever, which prevails in the Punjab, is often ushered in by such symptoms; without the microscope, its true nature may be hard to recognise.

Dysenteric form.—Another form of pernicious attack is characterised by the sudden appearance of dysenteric symptoms, perhaps by hæmorrhage from the bowel or elsewhere. The possibility of a suddenly developed dysentery being of malarial origin must therefore be kept in view; particularly if, in what appears to be ordinary dysentery, axillary temperature is found to be unusually high. In every case of dysentery of this description an examination of the blood should be made before the usual treatment for that disease is instituted—a treatment which, in the adynamic state the patient is probably in, might very well prove fatal.

Syncopal form.—In the preceding types of algide pernicious malarial attack the dangerous symptoms show themselves in the rigor stage of the fever. There is yet another form in which the danger appears

to depend on an exaggeration of the symptom usually hailed as bringing relief, and, for the time, freedom from danger. Thus the sweating of the stage of defervescence may be excessive and cause collapse which, if the patient rise up suddenly or make an undue effort, may lead to fatal syncope. Weak and cachectic patients, therefore, should be warned of this possibility, and not be permitted to rise suddenly or to exert themselves in any way during the defervescence of an ague.

The *pathology* of these various forms of algidity is probably of a very mixed character. In the gastric, choleraic, dysenteric types probably there is an accumulation of plasmodia in the vessels of the intestinal mucosa; such accumulations of parasites have been described. In those attacks in which profuse sweating is the dangerous element, the diaphoresis may be regarded, at all events in part, as symptomatic of excessive blood destruction—of what is, in reality, equivalent to a sudden and extensive hæmorrhage; or it may be that it is only an excessive reaction to the malarial toxin. The dangerous syncope attending all types of algidity is secondary, and merely an expression of collapse.

Hæmoglobinuric fever.

There is one form of what is believed to be malarial infection, which, though fatally common in certain countries, and though possessing very alarming and distinctive symptoms, has only comparatively recently been differentiated and studied. I refer to bilious hæmoglobinuric fever, sometimes erroneously called "hæmaturic fever," sometimes "blackwater fever."

This most dangerous disease prevails especially in the more malarial districts of tropical Africa. It was first described by French naval surgeons stationed at Nossibé, a French settlement off the north-west coast of Madagascar. Subsequently it was found to have a more extensive distribution, and to be common,

as mentioned, in many parts of tropical Africa. It is also found in the hotter regions of America, in the West India islands, in parts of the Eastern peninsula and archipelago, in the South of China, in Assam, and in some districts of India. Until quite recently, strange to say, no Indian writer had mentioned hæmoglobinuria as a feature in the pyretology of Hindustan or of the East. The disease occurs, but is rare, in South Europe, cases are sometimes met with in Greece and Italy. It was epidemic among the labourers employed in making the canal through the Isthmus of Corinth. Possibly it has been overlooked in many places.

There may be another explanation for the singular silence, on the subject of hæmoglobinuric fever, of the classical writers on Indian diseases; they may have confounded it with bilious remittent. It is difficult to believe, however, that the large number of acute observers who have studied Indian diseases so carefully, and for so many years, could have systematically overlooked this striking disease. Possibly, therefore, it is only of recent introduction into India. Such an idea is countenanced by the fact that certain medical men practising in Africa, good observers, declare that this form of malaria is of comparatively recent introduction there; and, moreover, that it is yearly becoming more common in that continent. There is another remarkable fact about hæmoglobinuric fever, which would lead us to believe that it is dependent on a form of the malarial parasite peculiar to itself; and that is, that in its recurrences malarial hæmoglobinuric fever often retains its peculiar characteristics for months after the patient has left the endemic area in which the germ was originally acquired.* Those who have suffered from it in Africa are liable not only to malarial attacks of the ordinary kind but to a recurrence of hæmoglobinuric symptoms for some

* Yersin and Breaudat assert that they found a special bacillus in the urine in several cases of hæmaturic fever. *Archives de Médecine Navale*, July, 1895, and June, 1896.

little time after their return to Europe; they may even die of it. I know of four such fatal cases which occurred recently in Great Britain, three in England and one in Scotland.

The European resident in tropical Africa regards three, or four, or more attacks of malarial fever as a regular feature in his *annus medicus*. Some of these attacks are of little gravity; others may be severe and inconvenient. On the whole, these attacks are not very much dreaded. When hæmoglobinuric symptoms declare themselves, however, such fevers are invariably regarded, and very properly so, with the utmost apprehension; for not only are they dangerous in themselves—at least one in every three or four proving fatal—but, even if recovered from, they leave the patient intensely anæmic, with damaged kidneys perhaps, and strongly predisposed to a recurrence of similar attacks in one of which he will probably succumb.

Hæmoglobinuric fever is not common during the first year of residence in Africa, though, in rare instances, it does occur even as early as the second or third month. It is usually after a year or two of malarial saturation, and after many attacks of an ordinary character, that it shows itself.

From statistics prepared from certain returns regarding the white employees of the Congo Free State, and from the evidence collated by other writers, it would seem that the third year of residence is the one most liable to this disease. Longer residence with immunity seems to imply in the European special resisting powers as against the diseases of Africa, and special suitability for the African climate. Native Africans, though subject enough to intermittents, enjoy a relative immunity from hæmoglobinuric attacks. This is not absolute, however; Easmon, Eyles, and Quartey-Papafio have recorded cases of the disease in natives. Many of the Chinese labourers on the Congo railway died of hæmoglobinuric fever.

Symptoms.—A European, who has been subject to occasional attacks of malarial fever which hitherto had been more or less successfully controlled by quinine, has a recurrence of what at first appears to be the familiar symptoms. A slight, or a more considerable rigor is followed by intermitting, or remitting, or irregular fever, with or without marked bilious symptoms. Earlier or later in the attack he becomes conscious of aching, perhaps severe pain, in the loins and in the region of the liver. In consequence of a somewhat urgent desire he passes water, when he is astonished to see that his urine has become very dark in colour, perhaps malaga-coloured, or possibly almost black. The fever continues, though not necessarily very high. Very likely he suffers from epigastric pain and distress, bilious vomiting to an unusual extent, and, it may be, bilious diarrhœa; or he may be constipated. The pain in the loins and the liver-ache continue, and the urine becomes darker and darker. By-and-by the sufferer breaks into a profuse sweat and the fever gradually subsides. (Fig. 20.) The urine, which hitherto had been somewhat scanty, now flows more freely; and, after passing

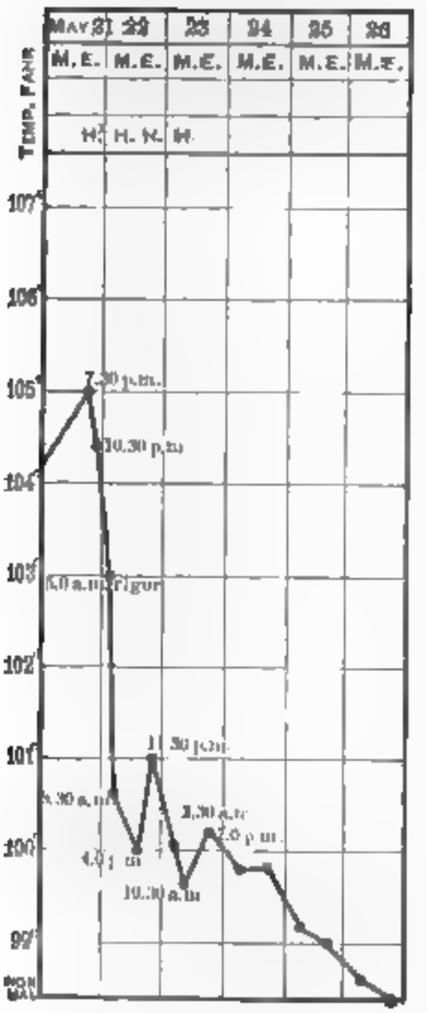

Fig. 20. Temperature chart of an attack of hæmoglobinuric fever occurring in England; infection acquired on the Congo. Recovery.

H, indicates hæmoglobinuria.

through various paling shades, from dark brown to sherry red, becomes once more natural in appearance. Coincidently with the appearance of the dark colour in the urine, or even before this has been remarked, the skin and scleræ rapidly acquire a deep saffron-yellow tint. This icteric condition persists, and even deepens during the progress of the fever, continuing for several days to be a striking feature in the symptoms. When the fever subsides, the patient is conscious of a feeling of intense weakness from which he recovers but slowly. Fever may recur next day, or for several days; or it may cease; or it may be remittent, or almost continued in type. The hæmoglobinuria may recur with each rise of temperature; or there may be only one or two outbursts.

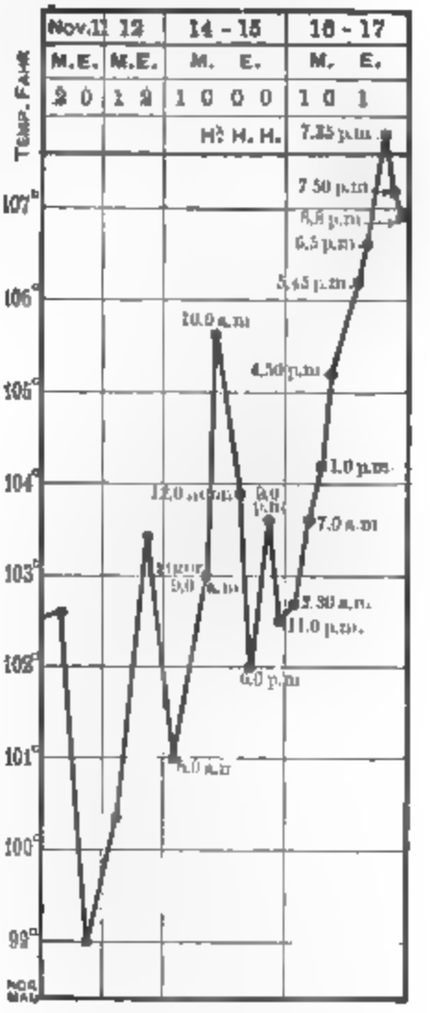

Fig. 21.—Temperature chart of recurrence of hæmoglobinuric fever in same patient (Fig. 20) shortly after his return to Congoland. Death.

H. indicates hæmoglobinuria

In the more severe forms of hæmoglobinuric fever there is usually a very great amount of bilious vomiting, of intense epigastric distress, and of severe liver- and loin-ache. The urine may continue copious and very dark in colour; or, continuing hæmoglobinous, it may gradually get more and more scanty, acquiring a gummy consistence, a

few drops only being passed at a time. Finally it may be completely suppressed.

In severe cases death is the rule. It appears to be brought about in one of three or four ways. The fever may assume the typho-adynamic type, or suddenly developed pernicious cerebral, hyperpyrexial (Fig. 21), or algide symptoms may supervene. In other cases the symptoms may be like those consequent on sudden and profuse hæmorrhage—jactitation, sweating, sighing, syncope. Or it may be that suppression of urine, persisting for several days, terminates, as cases of suppression usually do, in sudden syncope, or convulsions and coma. Or nephritis may ensue and the patient die from uræmic trouble three or four weeks after all signs of hæmoglobinuria and fever have disappeared.

Such is a brief and imperfect sketch of the symptoms of this, the most important of the African forms of malarial poisoning. It is a disease which, as this continent becomes more opened up and more frequented by Europeans, is bound to occupy a greater amount of attention from medical writers than it has hitherto done.

The urine. - If the characteristic dark brown urine of a hæmoglobinuric case be stood for some time in a urine glass, it separates into two well-marked layers: an upper of a clear though very dark port-wine tint, and a lower—perhaps amounting to one-half or one-third of the entire bulk—of a somewhat brownish-grey colour, and consisting of a sediment in which an enormous number of hyaline and hæmoglobin tube casts are to be found, together with a large quantity of brownish granular material. Epithelium is also met with; but blood corpuscles may be entirely absent, or very few in number. With the hæmoglobin there is also an escape of the serum of the blood, for the urine turns almost solid on boiling, and for some days after it has regained a normal appearance the urine will still contain albumen, though in gradually diminishing amount.

The kidneys. If the kidneys of a fatal case are

examined at an early stage of the disease, they are seen to be enlarged and congested, the tubules blocked with hæmoglobin infarcts, the cells laden with yellow pigment grains, and the capillaries with black malarial pigment. If the case survive for three or four weeks and then die of uræmia, the appearances are those of large white kidney.

The parasite.—The parasitology of hæmoglobinuric fever has hardly been worked at. Plasmodia have been found in the blood and organs; but their specific characters have not been accurately determined, further than that they are small, and rarely sporulate in the peripheral blood, belonging, doubtless, to some form of the crescent-forming malignant type. Considering the peculiar clinical manifestations it gives rise to, and the facts of geographical distribution, it seems likely that the parasite of malarial hæmoglobinuric fever is specifically different from the malaria parasites usually met with in Europe and, perhaps, in India.

A practical experience of these suddenly developed pernicious fevers of the tropics teaches that we should never make light of any malarial attack; particularly if it be of a mild irregular character and imperfectly controlled by quinine, and if small parasites, or the crescent form, be present. It further teaches that the subjects of such fevers should be particularly careful to guard against chills, fatigue, insufficient and unwholesome food, and all causes of physiological depression. The subjects of African hæmoglobinuric fever must exercise special caution in these respects, not relaxing their care, for some months even, after their return to a cold climate. If possible, they ought not to return to Africa.

TABULAR STATEMENT OF THE CHARACTER-

Modified from

	DURATION OF DEVELOPMENT.	MOVEMENT.	PIGMENTATION.
1. Benign quartan parasite	72 hours	Slight movement in the immature forms	Coarse grains; little or no movement
2. Benign tertian parasite	48 hours or less (in anticipating types)	Active amœboid movement in the immature and also in the middle-aged forms	Fine granules in immature forms, often in the larger actively swarming
3. Malignant pigmented quotidian parasite	24 hours	The unpigmented immature form very actively amœboid; less active when pigment accumulates	Very fine; later coalesces in one or two lumps; does not swarm
4. Malignant unpigmented quotidian parasite	24 hours or less	Very active amœboid movement	None
5. Malignant tertian parasite	48 hours	Active; the movement remains present in the pigmented bodies	Moderately fine; often shows oscillatory movement

ISTICS OF THE VARIOUS PARASITES.

Mannaberg.

Maximum Size.	Form of Spore Formation.	Number of Spores.	Crescentic Bodies.	Alterations in the Infested Blood Corpuscles.
The size of the red blood corpuscles	Daisy form; the single spores roughish, with distinct nucleolus.	6–12	None	The red blood corpuscles are little discoloured, and do not alter their size.
Size of the red blood corpuscles, sometimes even larger	Sunflower or grape-like, single spores small, round; nucleolus rarely seen	15–20 (often less)	None	The red blood corpuscles are often hypertrophied, and lose colour quickly and completely
¼–½ the size of a red blood corpuscle	Irregularly formed heap	6–8 (even more)	Present	The red blood corpuscles shrink often, and are then either darker-stained (copper colour) or may be completely decolourised.
¼–½ the size of a red blood corpuscle	Star-shaped, or in irregular heaps	6–8	Present	The red blood corpuscles shrink frequently, and are darkly stained
¼–½ the size of a red blood corpuscle	Irregular heaps	10–12, rarely 15–16	Present	The red blood corpuscles shrink frequently, they are darkly stained, or may be perfectly colourless.

CHAPTER III.

MORBID ANATOMY AND PATHOLOGY.

The blood in malaria. As the plasmodium is a blood parasite we naturally expect that the primary effect of its presence will be exercised on, and manifested in, the blood; and as the parasite lives in and at the expense of the corpuscles, destroying a certain proportion of them—in fact all those attacked we look, in the first instance, for a corresponding diminution in the number of these corpuscles an oligocythæmia.

Oligocythæmia.—Accordingly, when in malarial disease we come to measure accurately the corpuscular richness of the blood, we do find a decided oligocythæmia, and, not only this, but we find a degree of oligocythæmia greatly in excess of anything we might expect, or which can be accounted for by, or is in correspondence with, the proportion of corpuscles attacked and directly consumed by the plasmodium, judging by what we see in finger blood peripheral blood. If, for example, every hundredth corpuscle contains a parasite, we might look for something like a quotidian, tertian, or quartan 1 per cent. reduction in the total number of blood corpuscles; if every twentieth corpuscle contains a parasite—a very high and unusual proportion—we might look for a similarly timed 5 per cent. reduction.

Now this is an amount of hæmolysis which should be easily compensated by the latent physiological hæmogenetic margin, and which one would not expect to show itself as a definite anæmia, or to show itself only after the recurring drain had been kept up for some considerable time. But what are the clinical facts?

One or two paroxysms only, of some malarial fevers, may be immediately followed by an anæmia so pronounced as to be discernible to the eye in the intense pallor of the skin and visible mucous surfaces. On counting the corpuscles in such a case we note a regular drop in their number of from 5 to 10 per cent. per paroxysm. Often after a single paroxysm of some pernicious fever as many as half a million, or even one million, corpuscles per c.mm. drop out of the normal five millions, and this reduction may go on, as paroxysm follows paroxysm, until the corpuscular richness has fallen to one million, or even less.

Diminished hæmoglobin value of corpuscles. -Not only is there in many, in fact in most, cases of malarial disease a pronounced oligocythæmia, but there is, in addition, a marked diminution in the hæmoglobin value of the surviving corpuscles; it may fall 10, 20, or even as much as 50 per cent

Diminished amount of blood. And not only is there this marked diminution in the proportion of the corpuscles to the bulk of the blood and marked diminution in their hæmoglobin value, but there is, furthermore, in all malarial conditions of any considerable standing, a marked diminution in the volume of blood. Thus it comes that at the *post-mortem* examination of such a case we do not always meet with that congestion of the organs which is so usual a feature in most specific fevers. On the contrary, although in quite recent cases visceral congestion may be marked enough, if a malarial fever has been of any considerable duration, the venous system, with the exception of that appertaining to the spleen, liver and portal system generally, may be markedly empty. And thus it is that often, when we would make a preparation of blood from the living malarial patient, we may find that not only is the blood pale, lake-coloured, thin, and watery, but that it does not flow freely from the pricked finger.

Destruction and reparation of blood in first attacks

and in relapses. There appears to be no very definite or manifest law governing the degree, progress, and quality of the anæmia of malarial disease. On the whole, and as rough general rules, it may be laid down that in any given case the anæmia is in proportion to the severity of the febrile attacks; that although the loss of corpuscles following first attacks is usually very marked, this loss is rapidly made good; whereas, that although in relapses the loss of corpuscles is less pronounced, the tendency to reparation is also less.

Morbid anatomy: *Macroscopic.* If the body of a patient who has died in the course of an acute attack of malarial disease be dissected, certain appearances are generally found. In the first place, and invariably, the *spleen* is enlarged—often very much enlarged; its surface is dark—black sometimes, what is called pigmented. On section, the gland tissue is also found to be dark. Generally the parenchyma of the organ is so much softened as to be almost diffluent, so that the tarry pulp can sometimes be washed away by quite a gentle stream of water. The *liver*, too, is softened, congested, enlarged, and pigmented. The vessels of the *pia mater and brain cortex* are full, and the grey matter may present a peculiar leaden hue. The *marrow* of the spongy bones, such as the sternum and the bodies of the vertebræ, is also dark and congested; and a similar state of pigmentation and perhaps congestion may be discovered in the *lungs, alimentary canal, and kidneys.*

Microscopic: Malarial pigmentation.—The pigmentation referred to is pathognomonic of malaria. On submitting malarial blood from any part of the body to microscopical examination, it will be found to contain grains of black pigment. Particularly is this the case with blood from the organs just mentioned. If microscopical sections of these organs (Plate II., Figs 2, 3, 4) be examined there will be found, more or less thickly distributed in the blood, and within the endothelium of the arterioles and

capillaries, minute grains, or actual blocks, of the same intensely black substance. For the most part these pigment grains are enclosed in leucocyte-like bodies which are either clinging to the walls or lying loose in the lumen of the vessels. Here and there the pigmented bodies may be so aggregated together that they form veritable thrombi, and actually occlude the vessels. It is possible that many of these bodies are not pigmented leucocytes, but are really dead and breaking down parasites; for, if the body from which preparations were made be quite fresh—that is, if the preparations were made within two or three hours of death, it may be possible to see that the capillaries of some of the organs are full not only of pigment but also of plasmodia, a very large proportion of the blood corpuscles containing parasites. Particularly is this the case with the spleen and bone marrow; often, too, with the brain, liver, epiploon, and intestinal mucosa. The spleen and bone marrow are further distinguished from the other organs mentioned by the position in which the pigment occurs in them. In all organs the pigment is found in the blood vessels, but only in these two organs is it found in the cells of the parenchyma as well, and outside and away from the blood vessels. This extravascular pigment is either free, or it lies in the large cells characteristic of these organs, or in the small cells of the parenchyma.

Nature and source of malarial pigment. What is this black pigment which is so generally diffused throughout the circulation, and which is so specially abundant in the spleen and bone marrow? In colour, in structure, and in chemical reaction it corresponds exactly with the pigment already described as forming so prominent a feature in the malaria parasite itself. Like this, it is insoluble even in strong acids; it is altered by potash, and is entirely and rapidly dissolved by ammonium sulphide. It may occur as minute dust-like grains, or as coarser particles, or as agglomerations of these into irregular, mamillated

lumps. So far as the circulation is concerned, such a pigment is found in no other disease whatever. As an extra vascular pathological product it is found only in certain melanotic tumours; but only in the cells of the tumour, never in the blood vessels. Pigments of several kinds are found in old blood clots; but such are manifestly different from the pigment of malaria, and yield very different chemical reactions. Intra-vascular black pigment, therefore, is absolutely pathognomonic of malaria.* Because of its physical characters, and of the circumstances in which it occurs, it may with confidence be regarded as the specific product of the malaria parasite itself.

Source of the pigment in the pigmented leucocyte. If further evidence be required of the identity of the intra-parasitic pigment and that found in the tissues, it is supplied by a study of the fate of the pigment grains and clumps set free in the blood on the breaking up of the sporulating plasmodium.

If malarial blood, drawn during the rigor and early stages of acute attacks, be examined, leucocytes carrying grains or even blocks of black pigment will be encountered frequently. If the observer be fortunate and persevering, he will sometimes actually see whence this pigment is derived; he may even detect the leucocytes in the act of taking it up. He may see the pigment set free in the liquor sanguinis by the falling to pieces of a sporulating plasmodium: and he may then see a phagocyte creep across the field of the microscope and slowly engulf the little block. This undoubtedly is one source of the pigment in the leucocytes. Other, though possibly less important, sources, are the effete crescent bodies, and, very especially in the large cells of the spleen, necrosed parasite-containing red blood corpuscles.

Phagocytosis in the spleen.—The evidence of phagocytosis in the spleen in malaria is very remarkable.

* The pigment dot occurring in a large proportion of the lymphocytes, even in normal blood (see p. 26), must not be confounded with malarial pigment.

Not only are large and small masses of pigment included in the macrophages, in the smaller cells, and in the endothelium, but entire blood corpuscles—sometimes as many as eight or nine, mostly containing parasites—besides free parasites, free pigment, and fragmented hæmoglobin are frequently to be seen in one and the same phagocyte. Sometimes even one pigment laden phagocyte may be seen included in another phagocyte, and these perhaps in a third.

Blood of the splenic vein and liver.—There is one remarkable fact about the distribution of the pigment which requires mention. Of all the vessels of the body, the splenic vein is that in which malarial pigment is most abundant; and, whereas in other vessels it is found included in ordinary leucocytes, in this vessel the pigment is found included, not only in the leucocytes, but also in certain large white cells identical with those occurring in the spleen, and, doubtless, of splenic origin also. Similar cells may be found in the capillaries of the liver, rarely, however, in the blood beyond this organ; that is to say, they are filtered out by the liver from the blood carried to it by the splenic vein. An additional reason for the abundance of pigment in the splenic vein is, that not only is the spleen the physiological destination of many of the pigment-laden leucocytes and effete parasite-infested corpuscles, but it is likewise a favourite nursery for the plasmodium. In fact, the parasite is present in this organ in greater profusion than elsewhere. So it happens that the splenic vein, coming direct from a rich breeding- and dumping-ground for the plasmodium, contains a large number of pigment-laden leucocytes.

The plasmodium favoured by slow capillary circulation.—One reason for the marked predilection shown by the parasite for the spleen is probably the circumstance that the circulation in this organ is relatively slow, the vascular network, as compared with the arterial supply, being unusually rich and capacious, so that the blood tends to stagnate. It is

this condition of relative stagnation which seems to be favourable to certain types of plasmodia, and to determine their accumulation and relative abundance in special organs. Apparently it is for this reason that the plasmodium tends to abound in the liver, in the pia mater, the cerebral cortex, the bone marrow, the alveoli of the lungs, and in the villi of the intestine—all of them parts in which capillary capacity is relatively in excess of arterial supply. And, just as the parasite prefers a slow current, the pigment laden leucocytes also seem to linger and to settle down in these quiet backwaters of the circulation, and there to deposit their burden. Thus there is a double reason for the excess of pigmentation in the highly-vascular organs.

Extra-vascular pigment.—In the early stages of malarial disease, except in the case of the spleen and bone marrow, the pigment is entirely confined to the lumen of the vessels and to their endothelium. But if we examine tissues from a case which has died at a late period of the disease, the pigment may then be found, not only in the endothelium, but also in the walls of the vessels, and even in the perivascular lymph spaces, whence, it may be inferred, it is subsequently carried to the lymphatic glands, there to be finally dealt with and broken up. As encouraging this view about the ultimate fate of the malaria pigment, Kelsch has pointed out the significant fact that the lymphatic glands in the hilum of the liver are always markedly pigmented in old standing malarials; a fact evidently referable to the disposal of the large quantities of pigment which, as we have seen, the liver filters out, more especially from the splenic portion of the portal circulation.

These facts explain malarial pigmentation and oligocythæmia. The facts just mentioned explain not only the origin and nature of malarial pigmentation, but also, in part at least, the oligocythæmia of the malarial state, which, as pointed out, is only partially accounted for by the destruction of corpuscles by the

plasmodium in the general circulation as represented by finger blood. They show that what is seen in finger blood does not represent anything like the aggregate mortality going on among the corpuscles from direct destruction by the plasmodium. The principal part of the malarial drama is played out in the spleen, liver, bone marrow, brain, etc., and not in the general circulation. What is seen in finger blood is but an overflow, as it were, of the greater drama going forward in the viscera.

The yellow pigment. — Although the black pigment is so prominent a feature in malaria, it is not the only pigment of a pathological nature originating in the action of the plasmodium on the blood cells. The black pigment is a pathognomonic and interesting feature; but, apart from this, it does not seem to be of any really very great pathological importance. It does not seem to act as a poison, or irritant, or as a cause of degeneration of tissue, any more than a few grains of lampblack would, if so much. It is otherwise, however, with the pigment which Kelsch and Kiener have so carefully described, and which they call the "pigment ochre."

If the tissues of a patient who has recently died from a pernicious malarial attack are examined with a high power, there will be found (Plate II., Figs. 3, 4), in addition to the black pigment already described as lying in the vessels, another pigment—a yellow pigment—incorporated as little granules, or even as larger grains, in the protoplasm of the cells constituting the parenchyma of most of the organs and tissues of the body.

The yellow pigment not peculiar to malaria.—This pigment is not peculiar to malaria. It is found in other diseases and conditions, particularly in those associated with extensive and rapid liberation of hæmoglobin from the blood corpuscles. Thus it is found in paroxysmal hæmoglobinuria, in pernicious anæmia, in extensive burns, in poisoning by pyrogallic acid, potassium chlorate, arseniate of hydrogen,

and many other toxic agents. It has peculiar chemical properties, being equally insoluble in acids, in alkalies, and in alcohol. At first, when freshly deposited, it gives no evidence under the usual micro-chemical tests of containing iron; but after it has been in the tissues for some time it appears to be altered in character in this respect, and it then gives a ferrous reaction with ammonium sulphide, and with the double cyanide of iron and potassium.

Polycholia and hæmoglobinæmia.— Under ordinary conditions of physiological waste the products of the effete blood corpuscles are converted into bile pigment, and so got rid of. Up to a certain degree of pathological hæmoglobinæmia the liver can deal in a similar way with free hæmoglobin; and so it comes about that, when this substance is free in the blood in unusual abundance, the secretion and flow of bile become correspondingly increased. If this flow of bile be excessive, it gives rise to what are called "bilious symptoms"—bilious vomiting, bilious diarrhœa, symptoms which are so common in malarial disease, particularly in that variety known as "bilious remittent." Thus polycholia is a constant and often urgent feature in most malarial fevers, and is good evidence that in malarial infections there is a surcharge of the blood with free hæmoglobin. It is not improbable, although this point is disputed, that the yellowness of the skin and scleræ observed in these fevers is due to tinting by free hæmoglobin, to a hæmoglobinæmia in fact, and not, as is popularly believed, to biliousness or cholæmia from bile absorption.

The yellow pigment is deposited in excessive hæmoglobinæmia. As in those other conditions, referred to as being attended by rapid hæmolysis, in severe malarial fevers in which there is great and sudden liberation of hæmoglobin which the liver cannot at once deal with, pending its transformation into bile pigment the liberated hæmoglobin is taken up by the protoplasm of the cells of different parts of the

body and precipitated in them in a slightly altered form, it is stored up in fact, waiting to be worked off as bile pigment by the, for the time being, overtaxed liver. The yellow pigment, the "pigment ochre" of Kelsch and Kiener, is, in all probability, this precipitated hæmoglobin.

Great excess of hæmoglobinæmia results in hæmoglobinuria.—Should the liberation of hæmoglobin go beyond this, be too great and too suddenly effected for the excretory powers of the liver and the storage capacity of the tissues, then the hæmoglobin, little altered in character, seeks a more speedy way of escape by the kidneys, and hæmoglobinuria is produced. This is what is found in ordinary paroxysmal hæmoglobinuria, and in toxic hæmoglobinuria; and in this way we may account for the peculiar features of that most dangerous type of malarial poisoning, "bilious hæmoglobinuric fever."

Hæmoglobinæmia: how produced. How, it may be asked, does the malaria parasite give rise to hæmoglobinæmia, this liberation of hæmoglobin from the blood corpuscles? The enormous quantities of hæmoglobin free in the blood, deposited in the tissues, escaping in the urine, or elaborated as bile pigment, surely cannot be derived solely from the remains of the corpuscles invaded by the parasite, for these invaded corpuscles are almost entirely eaten up, and the hæmoglobin they once contained has been nearly entirely assimilated by the parasite and transformed into its proper tissue and into melanin.

It has already been pointed out that hæmoglobinometric observations show that in the surviving and non-infected corpuscles there is a pronounced deficiency of hæmoglobin. May it not be that part at least of the free hæmoglobin is derived from these corpuscles? May it not be that at a particular stage in all malarial fevers, at the stage of rigor (which, as has been explained, corresponds in time to the breaking down of the sporulated

red corpuscles, so much reduced in number and deteriorated in quality during the attacks.

The cause of fever and periodicity in malaria. The fever caused by the malaria parasite, and associated with the changes in the blood and tissues just described, is characterised by clinical features which, when typically manifested, clearly differentiate it from all other fevers. These features are, more especially, diurnal periodicity and intermission. Questions which suggest themselves in this connection are: What is the immediate cause of the fever in malaria? and, What is the reason for the remarkable intermissions, and peculiar, almost mathematical, periodicity which these fevers exhibit?

Febrogenetic agent.—In all malarial attacks this periodicity tends to become, and in most attacks actually is, quotidian, tertian, or quartan in type. If we study the parasites associated with these various types we find that they too, as has been fully described already, have a corresponding periodicity, the life of the individual parasite being completed in twenty-four hours, in forty-eight hours, or in seventy-two hours. Moreover, we have seen that the commencement of the fever in each case corresponds with the breaking up of the sporulating form of the parasite concerned. This last is an important point; for, doubtless, when this breaking up takes place, besides the pigment set free, other residual matters not so striking optically, it is true, as the pigment, but none the less real—are liberated, a hæmoglobin solvent, for example, as I have suggested. Whether it be this hæmoglobin solvent, or whether it be some other substance which is the pyrogenetic agent, certain it is that some toxin, hitherto enclosed in the body of the parasite, or in the infected corpuscle, escapes into the blood at the moment of sporulation; a pyrogenetic substance allied to the toxins of many of the pathogenic bacteria and to that of some animal parasites such as hydatids, bothriocephalus, and dracunculus. If, in addition to what is afforded by

the blood changes already described, proof be required of the existence of such a toxic substance, it is supplied by the fact that during the febrile stage of malarial attacks the toxicity of the urine is markedly increased. The fact that this toxin is liberated periodically accounts for the periodicity of the fever, as its successful elimination does for the intermission.

Theory of periodicity.—This is fairly evident and comprehensible. The parasites mature practically simultaneously. But how are we to account for the periodicity of the parasite itself? It is true that it has a life of twenty-four hours, or of a multiple of twenty-four hours; but why should the individual parasites of the countless swarm conspire to mature at or about the same time? That they do so—not perhaps exactly at the same moment, but within a very short time of each other—is a fact, and it is one which can be easily demonstrated. If we wish to see the sporulating forms of the plasmodium in a pure intermittent, it is practically useless to look for them in the blood during the later stages of fever, or during the interval, or during any time but just before, during, or soon after rigor. And if we wish to see the early and unpigmented forms, we must look for them during the later stage of rigor or the earlier part of the stage of pyrexia. And so with the other stages of the parasite; each has its appropriate relationship to the fever cycle. How is this simultaneity in the development of the individuals constituting the swarm of parasites to be accounted for?

Life-span of the parasite subject to variation.—It has already been hinted that the parasites do not all attain maturity at exactly the same moment; some ripen and break up a little earlier, some a little later. That the cycle for the individual parasite is not exactly and necessarily one of twenty-four hours, or of a multiple of twenty-four hours, is also certain; for it is a well-ascertained fact that fevers may

"anticipate" or "postpone"—that is to say, come on a little earlier or a little later in the day. Of course this means that the parasites "anticipate" or "postpone" Why in such cases should the parasites all anticipate together, or all postpone together; why should they all conspire to live either a little shorter, or a little longer; why should the swarm keep together, as it were? And, if the duration of the life of the individual parasite be thus subject to a certain degree of variation, why should not some of them mature a little earlier and others a little later; and so gradually, in the course of a few days, some of the different individuals constituting the swarm come to be maturing at every hour of the twenty-four, and thus every intermittent become a continued fever? In the answer to these questions lies the explanation of malarial periodicity.

Influence of physiological rhythm on malarial periodicity.—My belief and explanation of this matter is, that malarial periodicity does not altogether depend on the more or less definite life-span of the parasite, but that it depends, in part, on the well-known quotidian periodicity in the rhythm of the physiological processes of the human body.

Rhythmical immunity.—In all animals, including man, there exists a certain innate physiological protective influence, *qua* the malarial as well as other parasites. As regards malaria, in most animals this protecting power is absolute always sufficient, for no vertebrate animal, except man, so far as we know, is subject to malaria. But in the case of man this immunity is not quite absolute in every individual and at all times; although, as experience shows, in some men it is complete, and in many, with time, an increasing degree of protective power is gradually acquired. Thus in highly malarious countries the newcomer's first attack of fever is generally of the remittent or continued type; that is to say, the swarm of parasites is able to mature during a large part of the twenty-four hours, the protective power

being inoperative, or insufficient, for a considerable period, or for the entire circle of the day. But in the progress of a remittent malarial fever, even when untreated, the remissions tend to become intermissions — that is to say, the space of time during which the protective power of the body is insufficient tends to become contracted, although not altogether bridged over. As the physiological rhythm of the body is diurnal, the spacing of the fever to which this recurring susceptibility exposes the body is also diurnal. Should a proportion of the parasites in virtue of the variability which, as we have seen, they possess, mature earlier or later than this period of unprotection, they are destroyed by the still present or developing protective power, and the fever does not become continued. So it comes about that it is only the progeny of those parasites arriving at maturity during the rhythmically daily recurring insufficiently protected period which survive. In this way I seek to explain the phenomenon of malarial periodicity.

Spontaneous recovery. That there is a protective power in the human body against the plasmodium is certain, otherwise spontaneous recovery from malarial infection could not take place. Such spontaneous recovery is no unusual occurrence. A patient is attacked with typical malarial fever. He is admitted to a well appointed hospital. Plasmodia are found in his blood. He is kept without quinine. For one or two periods the fever comes off at the usual hour, and the parasites go through their typical course. But one day the parasites are seen to be fewer, and the next attack of fever is milder; thereafter fever does not recur again, and the plasmodia gradually and spontaneously disappear from the blood.

The only things that could be credited with the cure in such a case are the rest, the warmth, the good food, and the other favourable hygienic conditions of hospital life. The tonic influence of these things favours the rehabilitation of the self-defending physiological element of the body, and raises its amount,

quality and duration to such a standard of sufficiency that it is enabled to keep the multiplication of the plasmodium in check during the entire twenty-four hours. This defensive element may be, in part at least, no other than the phagocyte, which we have already seen to be an active agent in attacking and destroying the plasmodial spores on the breaking up of the mature parasites.

It is possible, therefore, that the intermittency observed in malarial fevers in great measure arises from two causes, the more or less fixed life span of the plasmodium, and the recurring diurnal deficiency or debility of a protective, plasmodium-destroying agency inherent in the human body. It might be urged that though such an explanation may be applicable to quotidian periodicity, it could not apply to tertian or quartan periodicity. This cannot be admitted. If there be a regular quotidian occurrence of susceptibility to the malaria germ, this susceptibility must be existent on the second and third day as well as on the first; therefore a tertian parasite, on maturing, will encounter it on the second day, and a quartan on the third, just as certainly as if they were daily maturing quotidian plasmodia.

Practical lessons from the hypothesis advanced. This hypothesis may be a wrong one. But although it may be wrong, it is not without its use if it impresses the importance of placing malarial patients under tonic influences as an aid to specific treatment; and, on the other hand, of protecting the subject of malarial recurrences from debilitating influences. For just as tonic influences may suffice to cure a fever, so, in many malarials, depressing influences, as a wetting, a surfeit, over-fatigue, anxiety, grief, in fact physiological strains of any description, are sufficient to provoke relapse of fever – presumably by debilitating or, for the time, abolishing the protecting physiological element which holds in check the latent but not quite extinct plasmodium.

CHAPTER IV.

MALARIAL CACHEXIA.

Definition.—Malarial cachexia is the term applied to a group of conditions, more or less chronic, the result of an antecedent attack of severe malarial fever, or of a succession of such attacks, or of prolonged exposure to malarial influences.

Symptoms.—The leading symptoms are those of a special kind of anæmia, characterised objectively by a peculiar earthy sallowness of skin, somewhat yellow sclerotics, enlargement of the spleen and—in the early stages at all events—of the liver. Usually the subject of this cachexia is liable to frequent attacks of an irregular type of fever, particularly after exposure or fatigue, or, in fact, after any unusual physiological strain.

Malarial cachexia without fever.—It should be mentioned, however, that fever is not a necessary antecedent or accompaniment of malarial cachexia. In highly malarious countries it is not unusual to see typical examples of this condition in which fever had never been a feature, or, at all events, had been of so mild a character as not to have seriously attracted attention.

Enlarged spleen.—In such countries a large proportion of the population have enormously enlarged spleens. The traveller cannot fail to be struck by the number of people he sees with big bellies and spindle shanks; by their languid and depressed air; their sallow, dry, rough, unhealthy-looking skins. In many malarial cachectics the skin pigmentation is remarkably dark; patches of almost black pigmentation are also sometimes discoverable on the tongue

and palate.* It is said that in some intensely malarial places children are occasionally born with enlarged spleens, as if the malarial poison had already affected them *in utero*. I cannot personally vouch for this, but I have often seen very young children with bellies enormously protuberant from distended spleen. According to Scheube, de Freytag and Van der Elst observed in 1873 and 1878 in Atchin that all the children born were affected at the time of birth with malarial cachexia, and that most of them died in a few months. Bein and Kohlstock found malaria parasites in the blood of the four months old child of a malarial mother, born some time after the arrival of the latter in a non-malarial district.

Delayed development In some instances of malarial cachexia of early development the general growth of the body is stunted and puberty retarded. I have seen a malarial cachectic who, although twenty-five or twenty-six years of age, had the stature and sexual development of a child of eleven or twelve. Abortion and sterility are common effects of malarial cachexia, which, in this and in other and more direct ways, becomes a potent agent in repressing population.

Acquired tolerance of the malarial toxin.—In many of these instances, although the state of cachexia has attained an excessive degree, ague, or, in fact, fever of any kind, has never been a prominent symptom. It would seem that the body can become accustomed to the fever producing toxin of the malarial parasite, much in the same way that it may become accustomed to opium and many other organic poisons, both animal and vegetable. I have watched for three weeks the rhythmical development of a tertian parasite in a sailor who, although previously the subject of frequent attacks of ague, was quite free from fever during the period I had him under close observation. Just as in those habituated

* Observations in India tend to show that this condition, melanoglossia, is racial and not pathological (*Indian Medical Gazette*, 1897)

to the use of opium, a full dose of the drug, which in the unhabituated would produce profound or even fatal narcosis, acts merely as a gentle stimulant; so in those constantly exposed to malaria from infancy the poison sometimes fails to act as a febrogene. And, to continue the comparison, just as the habitual use of opium produces a species of chronic poisoning or cachexia without narcosis, so the habitual presence of the malaria toxin may produce its peculiar cachexia without giving rise to fever. As a rule, however, particularly in the case of Europeans forced to reside in highly malarious countries, attacks of fever are of frequent occurrence in malarial cachectics.

Malarial neuroses and skin affections.—Superadded to the febrile attacks, and to the associated anæmia, we may meet in cachectics with a variety of functional troubles. One characteristic of most of these functional troubles is the periodicity they generally observe. Thus we may have quotidian or tertian neuralgias, gastralgias, vomiting, diarrhœa, headaches, attacks of palpitation, of sneezing, and so forth. Besides these, skin eruptions—such as herpes, erythema nodosum, patches of lichen planus, eczema, urticaria, etc.—exhibiting a quotidian or tertian liability to exacerbations and an amenability to quinine, have often been noted in malarial conditions.

Herpetic eruptions are very common in malarial attacks. According to Powell (*Brit. Jour. of Dermatology*, September, 1897), in Assam the appearance of a patch of herpes somewhere about the body is regarded as an infallible sign that the attack of fever is over for the time being.

Hæmorrhages.—In high degrees of cachexia hæmorrhages of various kinds are apt to occur—epistaxis, hæmoptysis, hæmatemesis, melæna, retinal hæmorrhages, purpura, occasionally hæmaturia or hæmoglobinuria. In such patients trifling operations—tooth extraction, for example—may prove a dangerous matter. I have seen in malarial cachectics, from the latter cause, hæmorrhage which was very difficult to

control; care must therefore be exercised in advising and in performing even the slightest operations in this class of patient.

Intestinal and pulmonary affections.—In addition to the troubles mentioned, we find that the subjects of malarial cachexia are apt to be dyspeptic; to suffer from irregularities in the action of the bowels; to suffer from morning diarrhœa, at first of dark bilious, and later, perhaps, of pale, copious and frothy stools. They are also very liable to a low and highly fatal form of pneumonia

Cachexia associated with functional and with organic lesion.—There may be said to be two degrees or kinds of malarial cachexia. In one there is merely anæmia with congestion of the portal system, this may be quickly recovered from on the patient being removed from endemic malarial influences and subjected to specific and proper treatment. In the other there is, in addition to anæmia, organic disease of the abdominal viscera—of the liver, spleen, and kidneys—the outcome of long-standing congestion of these organs. These tissue-changes not only keep up the anæmia, in spite of removal from malarial influences, but, in the long run, inevitably progress to a fatal issue.

Pathology and pathological anatomy.—The pathology of malarial cachexia is virtually that of acute malarial disease. There is blood destruction by the direct action of the malaria parasite and of its toxins, which eventuates in oligocythæmia and in the deposit of melanin and altered hæmoglobin (the yellow pigment) in the tissues; the activity of the process leading to congestion ending in organic changes in liver, spleen, and kidney.

Splenic enlargement. The spleen may become so enlarged under repeated attacks of the congestion attending a succession of fever fits, or in consequence of a less active and perhaps feverless hæmolysis, that it may come to weigh many pounds, and so to increase in bulk as to occupy nearly the

entire abdomen. The capsule of the gland, particularly on its convex surface, is thickened, and, perhaps, the seat of fibrous patches, or even of adhesions to neighbouring organs. Many of the trabeculæ forming the framework of the gland become greatly hypertrophied. On section, the tissues of such a spleen are found to be moderately firm, and usually of a reddish brown colour; but when death happens soon after or during a febrile attack, the section of the gland shows a dark surface from deposit of black pigment, the pulp at the same time being softened. Perhaps from over-distension some of the vessels in the interior of the gland give way, and then there is a breaking down of the spleen pulp in patches, the remains of splenic tissue floating about in the extravasated blood. Microscopic inspection of these hypertrophied spleens, especially during fever, shows the black and ochre pigments in the usual situations.

Splenic tumour in a district is indicative of endemic malaria. There are one or two practical points in connection with the malarial spleen which deserve mention. The prevalence, or relative absence of these enlarged spleens, or "ague cakes" as they are sometimes called, in the native population is an excellent rough indication of the salubrity, as regards malaria, of any particular district. Wherever they are common the district is malarious and therefore unhealthy, perhaps to Europeans deadly, and should be looked upon as extremely unfavourable for camping or residential purposes.

Liability to rupture of splenic tumours. Another practical point is that these enlarged spleens are easily ruptured by a blow on the belly. In hot and malarious countries many a coolie goes about doing his work although he has a spleen in his abdomen nearly twice the size of his head, which might be easily ruptured. This is a fact to be remembered in administering even mild corporal punishment to natives of malarious countries. Europeans have more than once been tried for manslaughter

in consequence of neglecting it. Owing to this liability to rupture, the subjects of splenic enlargement must not be allowed to play at violent games, as football or even cricket, or at any game in which the diseased organ is exposed to a blow. Apart from direct violence, an enlarged spleen may rupture spontaneously owing to sudden accession in size in the course of a fever fit.

Splenic ruptures are, of course, generally fatal. It sometimes happens that the presence of adhesions limits and restrains the hæmorrhage; localised hæmorrhages of this description may, in time, lead to splenic abscess.

Hepatic enlargement. Like the spleen, the liver in malarial cachectics becomes enlarged during accessions of fever. Under the influence of a succession of acute attacks, hepatic congestion may gradually acquire a more or less permanent character. After death from such fevers the capsule of the liver is found to be tense; on section, the highly vascular tissue of the organ is seen to be reddish brown or almost black, according to the degree and kind of pigmentation. If this state of congestion be long maintained, it tends to bring about various kinds and degrees of chronic hepatitis with hypertrophy of the interlobular connective tissues, and in time leads to hypertrophic, or to different forms of atrophic, cirrhosis. Thus irremediable organic disease of the liver, portal obstruction, and ascites may ensue.

Siderosis. It is in livers of this description that a form of what is called *siderosis* is produced—a condition resulting from chemical changes undergone by the yellow pigment with which the various cells of the organ are charged. It has already been stated that, when first deposited, this pigment gives no ferrous reaction with ammonium sulphide, or with the double cyanide of iron and potassium; and that, as the deposit becomes older, slow chemical changes ensue, resulting in the elaboration of a form of iron which will then yield the characteristic black colour with the former,

and blue colour with the latter reagent. Treated with ammonium sulphide sections of liver, and also of spleen, kidney, and other ochre-pigment-charged tissues from chronic malarials, may turn almost black to the naked eye or, at all events, exhibit abundance of blackened pigment on being placed under the microscope. In such sections it is seen that the ochre pigment is no longer in minute grains, as when first deposited, but in blocks and globules as large as, or even larger than, blood corpuscles. This pigment is, of course, something quite apart from the parasite-derived melanin deposited in the same organs.

Practical considerations.—Certain clinical facts about malarial hepatic congestion and malarial hepatitis are of importance. (1) Such conditions do not tend to terminate in suppuration; (2) they are almost invariably associated with splenic enlargement. These are important facts to recollect when it becomes a question of the diagnosis of malarial hepatitis from abscess of the liver. Another important fact to remember is that recent malarial enlargement of the liver is usually curable, depending as a rule on simple congestion; whereas old-standing malarial hepatic enlargement is usually incurable, depending, as it usually does, on hypertrophy of the connective tissue and a cirrhotic condition of the organ.

Malaria a cause of nephritis.—Changes similar to those found in the liver in the course of, and in consequence of, malarial disease occur in the kidney; in time they result in confirmed Bright's disease. Hence, probably, the frequency of Bright's disease in some highly malarious climates. In the *British Guiana Medical Annual,* Dr. Daniels mentions that in 926 *post-mortem* examinations in the hospital at Georgetown, Demerara, a highly malarial district, he found evidence of disease of the kidneys in no fewer than 228.

Cardiac degeneration.—As a consequence of defective nutrition from prolonged anæmia and recurring fever, the muscular tissue of the heart of chronic

malarials may degenerate, the ventricles dilate, and, in time, the lower extremities become œdematous.

Other sequelæ. — Dysenteric conditions, forms of diarrhœa, low forms of pneumonia readily set up by chill and prone to terminate in abscess of the lung or to become associated with empyema, extensive sloughing phagedæna, and other forms of gangrene such as noma, or pernicious fever, may supervene at any time and rapidly carry off the subject of advanced malarial cachexia.

CHAPTER V.

ÆTIOLOGY OF MALARIA.

Geographical range. — The geographical range of malaria is very great; it extends in the Northern hemisphere from the Arctic Circle to the Equator, and in the Southern probably as widely. Malaria is not uniformly distributed throughout this vast area. It occurs in limited endemic foci which tend, speaking generally, to be more numerous and larger as the Equator is approached.

Influence of latitude and season.—In colder latitudes the association of malaria with swamps is marked; in warmer latitudes this association is much less exclusive and apparent. In colder latitudes the type of disease is milder; in warmer latitudes it is apt to be more severe. In certain warm countries, however, as the Argentine and many of the islands of the South Pacific, malaria is entirely absent, or mild and rare. In colder latitudes it is active only during the summer or early autumn; in warmer latitudes it is perennial, certain seasons—usually, though not invariably, the warmer—being more malarial than others.

Influence of local conditions.—The strip of flat, waterlogged country lying along the foot of mountain ranges, the deltas of large rivers, the beds of dried-up streams, areas of country which have fallen out of cultivation, recently deforested lands, are, in many instances, notoriously malarial. Well-drained uplands and carefully cultivated districts, as a rule, are healthy. There are instances, nevertheless, of elevated, arid, and sandy plains which are intensely

malarial. Towns are much less malarial than villages or the open country.

Ship malaria.—Although several instances are on record of outbreaks of what was reputed to be malaria on shipboard on the open sea, many epidemiologists refuse to accept the diagnosis as to the nature of these outbreaks, and maintain that malaria is never contracted away from the land.*

Endemic and epidemic fluctuations.—From time to time malaria extends beyond its endemic foci, spreading in epidemic form over large tracts of what is usually healthy country. There are a few well-authenticated instances of countries (Mauritius, Réunion†) which, although previously exempt, subsequently became endemically malarial; and there are many instances of countries previously malarial which afterwards, especially under the influence of cultivation and drainage, became salubrious.

Atmospheric temperature.—One of the most important conditions necessary for the generation or, it may be, for the infective activity of the malaria germ, is a sustained average temperature of at least 60° Fahr.

Altitude.—A good deal has been written about the influence of altitude; but altitude *per se* has, apparently, no influence whatever. It is the decrease in temperature, usually implied by an increase in altitude, that is the real determining circumstance in bringing about a diminution in the prevalence of malaria in uplands. In the tropics an elevation of

* If it be the case that the malaria germ can be conveyed in water, it is conceivable that a ship's company may become infected by this means, and without direct exposure to telluric influences. I know of at least one instance of well-authenticated (microscopically) malaria occurring at sea which appeared to have been contracted in this way. If the malaria germ can be conveyed in water, my belief is that the same water quickly ceases to be infective; that is, that the germ does not live in water for more than a day or two. Hence, though a ship is supplied with water which might be dangerous to-day, if kept for a week the same water may be wholesome enough.

† Davidson, "Geographical Pathology."

six or seven thousand feet may not secure immunity from malaria unless there be, at the same time, a corresponding and sufficient lowering of temperature. In Italy there are many malarious spots high up among the hills; the same is the case in India and elsewhere in those elevated valleys which are also narrow, imperfectly ventilated, and imperfectly drained.

Moisture.—Another important condition for the production of malaria is the presence of moisture. In the Sahara there is no malaria unless in the oases; in many of these it is rife—in Biskra, for example.

Decomposing vegetable matter.—It is customary to add yet another condition as being necessary for the existence of malaria—namely, the presence in the soil of a notable amount of decomposing organic matter—particularly vegetable matter. But that this is not an indispensable condition is proved by the fact that there are many almost barren spots in which malaria abounds.

Other conditions necessary.—The concurrence of these conditions, high temperature and moisture, even though associated with abundant vegetation, is not sufficient to generate or support malaria; for there are many places in the world—the Argentine and the islands of the South Pacific, for example—in which high temperature, moisture, and decaying vegetable matter are present, but in which malaria is almost unknown. Manifestly there are other and more complicated conditions which are equally indispensable, and which must concur with heat and moisture in order to secure the presence of malaria. What these conditions are it is impossible to say. My belief is that they are in some way concerned with insect life, particularly with the mosquito, an insect which, as explained, there are strong reasons for regarding as the alternative host of the malaria germ, and necessary for its diffusion, as well as for its multiplication, outside the human body.

Influence of subsoil moisture.—The state of the

subsoil as regards moisture appears to have considerable influence on its malaria-producing properties. Short of general overflow, the higher the subsoil water the greater the chance of a given locality proving malarious. Hence the marked liability to epidemics of malaria on the subsidence of extensive floods; and hence the danger attending the raising of the level of the subsoil water by irrigation works, canals, embankments, and other engineering works.

These are facts which are manifestly compatible with, and which may receive their explanation from, the mosquito hypothesis of the extra-corporeal life of the plasmodium.

Disturbance of soil may give rise to malarial explosions.—It has often been observed that in malarious countries, so long as the soil remains undisturbed agues and the severer forms of fever are comparatively rare; but so soon as building, road-making, and other operations implying soil disturbance commence, then severe malarial fevers appear. After a time, and when these operations in the progress of events have concluded, and the broken surface of the soil has, so to speak, skinned over again, the place becomes once more comparatively healthy. The medical history of Hong Kong may be cited in illustration of this fact. At the commencement of the occupation of this island by the British, for a short time it was healthy enough. Then, on its cession being completed, and when barracks and houses were being built and roads laid out, it became excessively unhealthy, the soldiers dying by the hundred of pernicious fevers. In time the sickness and mortality gradually decreased; and now, so far as malaria is concerned, the city of Victoria is healthy. But, even at the present day, wherever in the outskirts in the course of the construction of houses, roads, forts, and similar works, soil is turned up, fever—often of a most pernicious type—is nearly sure to break out among those

engaged in the works. I cite the case of Hong Kong, but there are dozens of other instances which might be quoted, and which are quite as apposite and convincing as to the danger of disturbing the soil in malarious localities, particularly during the warm season

Influence of rainfall.—As regards the relation of the prevalence of malaria to rainfall there have been too many generalisations based on the limited experience of one or two districts. Thus, it is often said that the most malarious time of the year is at the end of the rains, when the soil is beginning to dry up. A wider view of the subject shows that, though applying to some places, this statement does not apply by any means to all There are localities where the fever curve is highest before the setting in of the rains. In some places, particularly in those that are low-lying, flat, and swampy, fevers of first invasion disappear almost entirely when the country becomes flooded. This apparent want of a universal and definite relationship of fever curve to rainfall indicates that the conditions determining the prevalence of malaria are highly complex, and that they are not by any means merely a matter of heat, moisture, and vegetation.

Influence of winds and atmospheric diffusion.—Another subject on which there has also been a large amount of loose generalisation is the relation of malaria to wind. It is said that the wind can carry the malaria germ great distances, roll it along the ground like thistledown, and even force it to ascend high mountains. It is very doubtful, however, if malaria can be transported, in this way, very far from its source. It is certain that some thousand or fifteen hundred yards of water between a ship and a malarious coast suffice to secure immunity to the crew. The circumstances of the notorious Walcheren expedition prove this. A similar distance on land from a malaria source is probably quite as effective. The diffusion of malaria by winds is probably extremely

restricted. Inside a city may be quite healthy, whilst outside the walls the country may be pestilential. One village may be sickly, whilst a neighbouring village may be healthy. Surely, if winds transport the malaria germ for any distance from its source, there would not be so great a difference in the relative salubrity of urban and suburban localities, nor of neighbouring houses and villages. Neither does the malaria germ ascend to any great height above the ground. Acting on the empirical observation of this fact, the peasants in many unhealthy spots in Italy and Greece secure a remarkable degree of immunity by passing the night, during the fever season, on platforms raised on poles a few mètres above the ground. It seems safe, therefore, to conclude that the horizontal and vertical diffusion of the malaria germ are very restricted.

As Ross puts it, a square yard of malarious soil a yard away is just as dangerous as a square mile of swamp a mile away. A puddle of water under a bedroom window is more dangerous than acres of rice fields some distance off, whether to windward or to leeward. The diffusion of the malaria germ is in no wise different in this respect from the diffusion of other infective disease germs —small-pox, typhus, scarlet fever; a very short distance from the infective focus secures immunity. It is as if the malaria germ, like the germs of those other diseases, perished after very brief exposure; or that it requires a high degree of concentration to be pathogenic. Lancisi misled us on this point.

Meteorological conditions in relation to relapses. —In estimating the healthiness and unhealthiness of a spot care must be taken to distinguish between fevers of first invasion, the result of recent infection and due to the existing immediate surroundings of the patient, and relapses, from non-specific causes, of a long antecedent infection. Fevers of the latter description are often met with in non-malarial Britain, particularly in the winter time. A malarial subject

while in the mild climate of the tropics may keep in fair health; but when he is plunged into the stormy winter of the North, is exposed to cold, and has long watches and fatiguing work, very probably latent malaria will become active and ague follow. This is a common experience with malarials from the tropics. It is almost the rule with people coming from the West Coast of Africa. Stanley says that so long as he and his companions were ascending the Congo, the wind being with them and therefore not much felt, they did not have fever; but that on descending the stream, a strong breeze blowing in their faces and chilling them, they constantly had attacks. The physiological depression and disturbances caused by the cold wind paralysed the self-protecting power of the body, and permitted the hitherto latent plasmodia to get the upper hand. And so it is found, in the highly malarious districts of tropical Africa, that houses perched on elevated and windy situations are not so healthy as those on lower and, therefore, less exposed and more sheltered ground. This latter fact must not be interpreted as showing that wind causes or carries malaria. The wind merely acts as a cause of physiological strain, of chills; it acts just in the same way as fatigue, hunger, a wetting, disease, fear, or depressing emotions might do. Malaria can be contracted only in close proximity to the extra-corporeal nidus of the malaria.

Time of day in relation to infection.—For some obscure reason, possibly, as is generally supposed, connected with alterations in atmospheric movement, with expansions or contractions of the air, exhalations or precipitations brought about by rapid changes in the relative temperatures of the soil and atmosphere incident to this particular time in the twenty-four hours, the periods just before sunrise and just after sunset and the night have the reputation of being the most dangerous as regards liability to contract the infection. To those actually engaged in the work, the risk from earth disturbance

seems at times to extend throughout the twenty-four hours.

Bignami, who believes that the mosquito is an active agent in conveying malaria to man, explains the greater danger of night exposure in malarious localities by the supposition that the germ is directly introduced by the bite of this insect, which, as is well known, is mainly nocturnal in its habits. Although I do not agree with this view of the *modus operandi* of the mosquito, nevertheless, I think that, in view of Bruce's notable work on the tsetse fly as a medium in diffusing the trypanosoma of "fly disease," and of the *rôle* of the tick in diffusing the Texas cattle fever, this idea of Bignami's should not be lost sight of. The general belief, however, is that the malaria germ enters by the mouth—is inhaled; but as to whether it subsequently gets access to the circulation through the air passages, or whether it is swallowed with the saliva, there are as yet no data to guide us to a trustworthy conclusion. Neither can it be said that the possibility of infection by drinking water has been either proved or disproved.

ACCLIMATISATION.

Personal acclimatisation.—Is there such a thing as acclimatisation as regards malaria? The answer to this is, "Yes and No." It would seem that those who have resided many years in a malarious district are less liable to severe remittents but more liable to mild agues. As already mentioned, the first attack of malarial fever is generally remittent and severe in character; subsequent attacks are generally frankly intermittent. Old febricitants are more liable to pernicious attacks of an adynamic type than the recently infected, notably to hæmoglobinuric fever Trifling causes, such as do not provoke fever in the fresh arrival, are often sufficient to bring on an ague fit in the old resident. The new arrival in the tropics does not think much of exposing himself to the sun, the rain, and the wind; but the old resident is very

chary about going out without his sun-hat and white umbrella. The latter wears flannel, and changes his clothes after exercise; he is careful not to cool off too rapidly by sitting in a draught; he will not sit down in wet clothes. The newcomer may look on these precautions against chill as signs of effeminacy. They are not so, however; experience has taught the old resident that neglect of them means an attack of fever and a week off work. The newcomer takes a cold bath; the old resident takes a warm one. The newcomer sits up late, eats and drinks and smokes as in Europe; the old resident goes to bed betimes, and eats and drinks and smokes in moderation. By-and-by, sharp lessons teach the newcomer to respect the sun and the rain and the wind, to clothe with a view to avoiding chill, to live temperately. This is an education all pass through in malarial countries. Acclimatisation, to a great extent, means experience —education; not simply an unconscious adaptation of the physiology of the individual but an intelligent adaptation of his habits.

Racial differences of susceptibility.—Nevertheless, there can be no doubt that, for some occult reason, certain races and certain individuals are less susceptible to malarial influences than others. It is a well-established fact that the negro in Africa, although he does get fever, yet he does not get it so frequently nor so severely as the European; even although the latter, from his hygienic ways of living, is of the two much the less exposed to infection. The Chinese, the Malays, and some other dark-skinned races also appear to enjoy a comparative immunity; an immunity considerably less pronounced, however, than that enjoyed by the African and West Indian negro. The inhabitants of the malarious districts of Italy, Corsica, Greece, Turkey, and many other South European countries have inherited no marked immunity from malaria in virtue of the thousands of years during which their ancestors lived in malarious districts. But they have inherited

experience, and many of them know how to keep clear of the infection they cannot overcome; this probably is, in great measure, the extent of their acclimatisation and apparent acquired immunity.

Sex, age, occupation.—Sex, *per se*, seems to have no particular influence as regards liability to, or severity of, malarial attacks. Neither has occupation; although, of course, those engaged in tilling and working the soil are more exposed to malaria, and therefore more subject to its manifestations, than the townsman or the sailor. Malarial attacks are more severe, more common, and much more dangerous in young children than in adults.

CHAPTER VI

DIAGNOSIS AND TREATMENT.

The three diagnostic signs of malaria: their respective values.

THE diagnosis of malarial disease, usually not a difficult matter, is sometimes very hard indeed. Formerly periodicity and the effect of quinine were the tests principally relied on. They are very fallible, however. Nowadays, in all doubtful and serious cases, it behoves the practitioner to have recourse to the only infallible test of malaria—the microscopic examination of the blood. When such an examination yields a positive result, when the plasmodium in any of its forms, or its product—malarial melanin—either free in the serum or enclosed in leucocytes, is found in the blood, the diagnosis of malaria is securely established. Negative results from a single microscopical examination are not so trustworthy as positive; but if the practitioner has experience, and if he has the opportunity to make his examinations at suitable times and in a case untreated by quinine, they too are conclusive.

The **quinine test** is generally conclusive in intermittents and in the various larval forms of malaria, but the more severe types of remittents are often singularly resistant to the drug. Time may not be available in which to test such cases with quinine. They may be cases of a threatening nature in which a speedy diagnosis is of the first importance. In such cases the microscope is the only trustworthy diagnostic agent.

Periodicity in diagnosis.—Periodicity is, of course, at times a trustworthy enough clinical test for

malarial disease. *Tertian and quartan periodicity occur only in malarial disease;* when either is thoroughly established, its presence is almost conclusive as to the case being malarial. But it is otherwise as regards the significance of quotidian periodicity. Quotidian periodicity we find in greater or less degree in nearly all fevers, particularly in fevers associated with suppuration. In hectic conditions, quite unconnected with malaria, one often sees a quotidian afternoon rigor, followed by hot, dry skin, and a temperature rising even to 103° Fahr. or 104° Fahr., the febrile movement concluding with a profuse diaphoresis and complete morning apyrexia.

Periodicity of fever in liver abscess; diagnosis from malaria.—Particularly is this the case in suppuration connected with the liver; and this is just a condition which is very liable to occur and to cause confusion in tropical practice Simulation of malarial fever by hepatic abscess is very common; it is a pitfall into which the inexperienced tropical practitioner often tumbles. In consequence, we find that most liver abscess cases are drenched with quinine, at one time or another, on the supposition that the associated fever is malarial. There are three or four points, however, even apart from an examination of the blood, which, if duly considered, should keep us clear of this blunder. In hepatic abscess the liver is enlarged, but the spleen is not necessarily so; splenic enlargement, though an occasional, is not a usual feature in liver abscess. In malarial fever, if the liver be enlarged the spleen is still more so and can nearly always be felt extending well beyond the costal margin. In hepatic abscess the fever occurs usually, though not invariably, in the late afternoon or evening, and the patient may perspire profusely at any time of the day or night—very generally whenever he chances to fall asleep. In malarial fever the paroxysm may, and generally does, occur earlier in the day, and there is no marked tendency to sweat unless

at the defervescence of the fever. In hepatic abscess, if carefully inquired for, there is nearly always a history of dysentery obtainable. If fever be distinctly tertian or quartan in type, it is not hepatic. In all doubtful cases the blood must be examined once or oftener, the rigor stage or early hot stage being selected for the examination, and the examination being made before administration of quinine. Occasionally cases are met with in which there is a history of malarial infection and, in addition to this, a history of dysentery, and the liver and spleen are both enlarged In such cases diagnosis may be impossible without the microscope and the aspirator.

Diagnosis of hæmoglobinuric from yellow fever. The diagnosis of hæmoglobinuric fever from yellow fever sometimes comes up as a practical point. Apart from microscopical examination of the blood, the following considerations will aid to a correct conclusion. From the outset hæmoglobinuric fever is asthenic in type, yellow fever, on the contrary, has sthenic features to commence with violent headache, congested conjunctiva, flushed face, etc In hæmoglobinuric fever the liver and spleen are enlarged, often painful, the vomiting is bilious, rarely bloody; the yellowness of the skin concurs in point of time with the hæmoglobinuria, and is an early symptom. In yellow fever there is early and increasing albuminuria, sometimes hæmaturia, but there is no true hæmoglobinuria, no enlargement and tenderness of the liver and spleen of a marked character. In yellow fever there is epigastric tenderness and burning; often vomiting of clear acid mucus, but not of large quantities of bile as in malarial affections. Black vomit and yellowness of skin are late and not necessary features in yellow fever Then yellow fever is endemic only in certain limited areas, tends to occur as an epidemic, and attacks newcomers much more frequently than old residents. Hæmoglobinuric fever has a more extensive distribution, is sporadic, and is more especially a disease of older residents.

Diagnosis of bilious remittent from yellow fever.—In bilious remittent the icteric tinting of the skin is an early feature; albuminuria is rare, and not a marked feature; temperature is maintained high for many days, not subsiding in three or four days as in yellow fever; the vomiting is profuse and bilious; the pulse does not become slow as in the later stages of yellow fever; the eyes are not congested and shining to the same degree; and, of course, the plasmodium is to be found in the blood.

Cerebro-spinal meningitis may simulate malarial fever; but the occurrence of rigidity of the muscles of the neck should put the physician on his guard, and lead him in such a case to search the blood and inquire for other diagnostic symptoms.

Diagnosis from other types of paroxysmal fevers.—Urethral fever is often mistaken for ague; so is the fever attending the passage of gall-stones; so is the fever associated with pyelitis and surgical kidney; so is lymphangitis, particularly that form of lymphangitis associated with elephantiasis and other filarial diseases; so is Mediterranean fever; so are the fevers associated with tuberculous disease, with ulcerative endocarditis, with some types of pernicious anæmia, with splenic leucocythæmia, especially with visceral syphilis, with rapidly-growing sarcoma, with forms of hysteria, and with many obscure and ill-defined conditions. The use of the microscope must not be neglected in such cases if there be the slightest doubt as to their exact nature.

Typhoid fever.—Without the microscope it is sometimes impossible to diagnose typhoid types of malarial fever from genuine enteric. In both there may be diarrhœa; in both there may be splenic enlargement; in both there may be typhoid tongue, delirium, and the entire range of typhoid symptoms. As a matter of fact, until recent years all typhoid in India was regarded and treated as malarial fever—malarial remittent—and, doubtless, often with disastrous results. In circumstances where Widal's

serum test can be used it is invaluable in such cases.

Typho-malarial fever.—One important fact in connection with the diagnosis of typhoid in malaria must ever be kept in mind. In individuals who have previously been subjected to malarial influences and who, perhaps, have suffered at one time from well-marked malarial fever, the oncoming of typhoid is often preceded by three or four paroxysms exactly like those of ordinary ague. This may occur even when the patient has been for several years in a non-malarial country, as England. In such cases quinine is usually given early in the attack; its failure to check the disease should lead to careful prognosis and the avoidance of too active purgation. Similarly, well-marked malarial-like fluctuations of temperature and the appearance of the plasmodium in the blood in the course of a continued fever do not exclude typhoid. These cases are typho-malarial, and have to be treated as such—as typhoid with a malarial complication.

Necessity for microscopical examination of blood in pernicious attacks.—Without the microscope it is sometimes impossible to diagnose, in time to direct treatment, pernicious comatose malarial attacks from heat-stroke or, if algide in character, from ordinary apoplexy; malarial dysentery, which must be treated with quinine, from ordinary dysentery, which must be treated with ipecac. or with the sulphates; algide malarial attacks, from cholera; certain types of malarial fever occurring, as it is very apt to do, in the puerperal state, from puerperal fever; malarial pneumonia, from crupous pneumonia; malaria aphasia, from the aphasia of organic brain disease; and so on.

It is manifest that the revelations of the microscope have enhanced our powers of diagnosis in malarial affections enormously, and, therefore, our powers of treatment. Every doubtful case must be tested by it. In many forms of malarial disease, if life is to be saved, action must be prompt, decisive,

energetic, and based on accurate diagnosis. The diagnosis of ordinary agues may be postponed for a day or two without much danger, and be diagnosed correctly enough without the microscope; but every now and again a pernicious attack is sprung upon the practitioner, the nature of which he must be able to recognise at once, and recognise with confidence. When the plasmodium is seen in the blood, it is surely known that there is a malarial element in the case and that quinine is indicated. Confidence in directing treatment is a great matter. It cannot, therefore, be too strongly urged on the tropical practitioner to avail himself of every opportunity to gain experience in the use of the microscope in blood examinations, and that he should take care to have a suitable instrument in working order and available at a moment's notice. The practical difficulties in carrying out this recommendation are insignificant in comparison with the importance of the results. With practice, five minutes usually suffice to effect a positive microscopical diagnosis of malaria.

TREATMENT.

Quinine.—Many drugs have been employed in the treatment of malarial disease, and many drugs have some influence on it; all sink into insignificance in comparison with quinine. In serious cases, to use any drug to the exclusion of quinine is culpable trifling. Therefore, so soon as a diagnosis of malaria has been arrived at, unless there be some very manifest contra-indication, the first duty of the practitioner is to set about giving quinine. There are many ways of exhibiting the drug; however given, care must be taken that it is given in such a way that there can be no mistake about its being absorbed. If the patient for any reason, such as inability to swallow or persistent vomiting, cannot take quinine by the mouth, and the existing condition be grave, it should be injected by the rectum; but if the circumstances of the case are such that a rapid action of the drug

is imperative, it must be injected at once subcutaneously, or into a vein.

When and in what dose to give quinine in ordinary cases.—During a paroxysm of ordinary intermittent fever, it is better, before giving quinine, to wait until the rigor and hot stages are over, and the patient is beginning to perspire. A fever fit, once begun, cannot be cut short by quinine, and to give quinine during the early stages aggravates the headache and general distress; but so soon as the skin is moist and the temperature begins to fall, the sooner the drug is commenced the better. Ten grains, preferably in solution, should be administered at the commencement of sweating, and thereafter five grains every six or eight hours for the next two or three days. This is almost a certain cure. The quinine may not always prevent the next succeeding fit, but it nearly always diminishes its severity. In 99 cases out of 100 the second following attack does not develop.

When giving quinine, it is well to administer an aperient and to keep the patient in bed; in ordinary cases neither aperient nor rest in bed is absolutely necessary. In cachectics, however, and in all obstinate cases, both are invaluable adjuvants. On the complete subsidence of fever, iron, or iron and arsenic, should be exhibited; and, with a view to prevent relapses, one or two full doses of quinine—five to fifteen grains—should be taken at intervals of from five to seven days for six weeks or thereabouts.

My practice in the treatment of ordinary malarial fevers is to give quinine for two or three days in the doses mentioned, and then to prescribe arsenic and iron in pill or solution. At the same time, with a view to prevent recurrence of fever, I direct the patient, particularly if I have found the crescent form of the parasite in the blood—for such cases are prone to relapse—to leave off the tonic one day a week (to give precision to my directions I generally mention Sunday) and on that day to take a mild

saline, sulphate of soda or Carlsbad salts, in the morning, and three five-grain doses of quinine during the day. The iron and arsenic may be taken for a fortnight at a time, and, after an interval of a week, for another fortnight. The weekly aperient and three doses of quinine had better be kept up for six weeks or two months.

Dose of quinine: toxic effects.—There is great difference of opinion and practice about the dose of quinine. Some give thirty grains at a dose, some give three. The former, in my opinion, is too large a quantity for ordinary cases, the latter too small. It must never be lost sight of that occasionally quinine in large doses produces alarming effects; not singing of the ears and visual disturbances merely, but actual deafness and even amblyopia, both of which may prove very persistent and occasionally permanent. It may also produce profound cardiac depression, and even death from syncope. Urticaria is another, and not very uncommon, effect of even small doses of quinine; some cannot take it on this account, and prefer to endure the disease rather than suffer the intolerable irritation induced by the remedy. I believe that nothing is gained by excessive doses; in ordinary circumstances, thirty grains spread over two or three days is usually amply sufficient to check an intermittent.

For children under one year half a grain for a dose suffices; for older children the dose must be increased proportionately to age and strength.

If a supposed ague resists the doses of quinine mentioned, it is advisable to revise the diagnosis.

Quinine in pregnancy.—Care should be exercised in giving quinine to pregnant females, for undoubtedly it sometimes causes miscarriage. The fact of pregnancy, however, must not debar the use of the drug altogether; only, in such circumstances, it should be given in the minimum dose likely to be effectual, say three grains repeated every eight hours for two days. A pregnant woman will run more risk

of miscarriage and to her health from repeated ague fits than she will from a reasonable dose of quinine.

Quinine in the puerperal state.—It is a wise precaution in malarious countries to give a few five-grain doses of quinine during labour or soon after. The puerperal state seems to have the effect, as any other shock or physiological strain might, of waking up the slumbering plasmodium. A dose or two of quinine in these circumstances does no harm, and may, by choking off a threatening fever, avert suffering and anxiety, not to mention danger.

Form in which to administer quinine.—Quinine is best given in solution, and probably the hydrochlorate, as containing a larger proportion of the alkaloid than the sulphate, is the best salt. Some, under the impression that hydrobromic acid prevents the ringing of the ears attending the free use of the drug, prefer it to dilute sulphuric acid as a solvent for the ordinary sulphate. When the tongue is fairly clean and digestion not altogether in abeyance, the quinine may be given in freshly prepared pill or in tabloid form; but in serious cases, particularly where the tongue is foul and digestion enfeebled, pills and tabloids are not to be trusted to; *in these circumstances they are apt to pass through the bowels and to appear in the bedpan unaltered.* In grave cases this occurrence must not be risked.

Milk as a menstruum for quinine.—If the taste of the drug be very much objected to, a good plan is to give it in powder in a tablespoonful of milk after the patient has previously lubricated the mouth with a morsel of bread and butter. In this way the bitter taste is not perceived. This is by far the best way of getting children to take quinine.

Hypodermic injection of quinine.—In any type of fever if vomiting is persistent, if the brain is affected, or if the patient is insensible and cannot or will not swallow, and, also, if the rectum is irritable, recourse must be had to the hypodermic

injection of quinine. In all cases in which life is in imminent danger, and in which the earliest possible action of the drug is of importance, it must be given hypodermically. This method of giving the drug is sometimes a painful one, and may be attended with some risk of abscess; in the circumstances, such possibilities count for little. The most suitable salt for hypodermic injection is the hydrochlorate or, better, the acid hydrochlorate, which is soluble in less than its own weight of water. The hydrobromate is equally soluble. If neither of these salts can be procured, the sulphate may be used, solution being effected by adding half its weight of tartaric acid. Ten to fifteen grains dissolved in sterilised water would be a full hypodermic dose; in grave cases this dose should be given three times in the twenty-four hours. The needle should be driven well home, either deep into the subcutaneous connective tissue or, better, into the muscles of the gluteal or scapular region, the skin being previously carefully cleansed. The solution must be freshly prepared and boiled, and the syringe and needle thoroughly sterilised. In the malignant fevers of Rome as much as a drachm of quinine, divided into three or four doses, is sometimes administered in this way in the course of twenty four hours.

Benson (*Trans. First Indian Med. Cong.*), speaking from an experience of 1,390 cases, says that the hypodermic injection of quinine is by far the most effectual, as well as economical, way of treating malarial fevers. He used the sulphate dissolved in water with the aid of hydrochloric acid, the strength of the solution being fifteen grains to the drachm, of this he injected twenty minims between the scapulæ, or into the outer surface of the arm. In 614 consecutive cases so treated not a single untoward accident occurred, one injection usually sufficing. Dr George Watt mentions a case of eight years' standing, which had been treated unsuccessfully by quinine in the usual way, and which was promptly cured by

hypodermic injections. Benson also succeeded in the same way in obstinate cases.

Hypodermic injection of quinine; precautions against tetanus. It may be well to mention, not with the idea of deterring the practitioner from using the drug in this way, but to impress upon him the necessity for care in keeping instruments and solutions aseptic, that tetanus has sometimes followed the hypodermic injection of quinine. In these unfortunate cases it was not the quinine that caused the tetanus; it was the tetanus bacillus, and this tetanus bacillus was introduced either on a dirty needle, or in a fouled solution. Tetanus is an exceedingly common disease in some tropical countries. In Western Africa, for example, a large proportion of wounds, no matter how trifling as wounds they may be, if they are fouled by earth or dirt result in tetanus. The French in Senegambia have found this to their cost. A gentleman who had travelled much in Congoland told me that certain tribes poison their arrows by simply dipping the tips in a particular kind of mud. A wound from these arrows is nearly sure to cause tetanus. In many tropical countries, so general and so extensive is the distribution of the tetanus bacillus that trismus neonatorum is a principal cause of the excessive infant mortality. Every precaution must therefore be taken to ensure that the little instrument, which is so potent in saving life, may not by carelessness be turned into an instrument of death.

Intravenous injection of quinine.—In cases of pernicious comatose remittent, in which it is of importance to obtain a rapid and concentrated action of the drug, Bacelli recommends the intravenous injection of the following solution: Hydrochlorate of quinine 1 gramme, sodium chloride 75 centigrammes, distilled water 10 grammes. This solution he has employed in those desperate cases with much success, injecting directly into a vein five to seven grammes at a time, he states that whereas with hypodermic injection the mortality in such cases mounted to

17 per cent., with intravenous injection it was reduced to 6 per cent.

Warburg's tincture.—A very effective medium for giving quinine and one of high repute in many places, is Warburg's tincture. This contains, besides quinine a number of drugs, many of them doubtless inert, although some of them certainly possess valuable therapeutic properties. Experience has shown that the combination is really a good one, and that Warburg's tincture sometimes succeeds where quinine alone fails or acts too slowly. It generally proves a powerful sudorific. The dose is half an ounce, and is repeated after two or three hours. The action appears to be somewhat similar to that of the antipyretics now in vogue—antipyrin, phenacetin, etc.—drugs which, when given in combination with quinine in the routine treatment of malarial fevers, sometimes contribute very markedly to the relief of headache and febrile distress.

Mode of action of quinine.—In what way quinine acts has not yet been satisfactorily explained. Some, reasoning from the toxic influence this drug exerts on all kinds of free amœba, say that it acts in malaria in the same way—that is, as a direct poison to the plasmodium. Others maintain that it acts by stimulating the phagocytes, stimulating the natural enemies of the parasite. Some experimentalists allege, on the other hand, that it paralyses the white corpuscles. That quinine does not kill all blood protozoa is certain, for it has no effect on the plasmodium-like organisms found in the blood of birds and reptiles, or on the trypanosoma of surra. Certain it is that in man, with the exception of the crescent body, it quickly causes the plasmodium to disappear from the general circulation. It is said by some to be most effective against the free spores of the malarial parasite and the very young intra-corpuscular forms, [illegible] active against the more mature plasmodia; [illegible] advocate giving it early in the plasmodial [illegible] hers, on the contrary, maintain that it is

operative only on the large intra-corpuscular stage of the plasmodium, and therefore advocate its use at a late stage of the cycle. It does not appear to have any effect on the crescent bodies, or to interfere with their evolution into flagellated organisms. As stated, I have seen in the blood crescents and flagellated bodies three weeks after the cure of a malarial fever by full doses of the drug continued for a fortnight.

Strange to say, quinine, especially in small doses, seems sometimes to wake up latent malaria and to bring about an ague fit. The same may be said of a course of mineral waters, of hydropathic treatment, and of sea-bathing.

Treatment of bilious remittent.—In bilious remittent and other severe forms of malarial fever one must not, as in a simple intermittent, wait for the remission before giving quinine. To wait for remission or sweating used to be the practice; it was said that to give quinine at any other time was wrong, and that something terrible would happen if the superstition were ignored. *In all grave fevers, a full dose, ten or fifteen grains, should be at once administered.* It is desirable to have the bowels freely opened; quinine is said to act better then. It is a mistake, however, to delay the administration of the specific pending the action of the aperient. If an aperient be indicated, it should be given along with the quinine. Five or ten grains of calomel is the best. Thereafter the quinine, in five grain doses, should be repeated every three or six hours until fever has subsided. If there be much bilious vomiting, an emetic of ipecac. or of hot water will clear the stomach and perhaps, after a time, enable it to retain the quinine. The drug is sometimes more readily retained if given in chloroform water. Mustard poultices to the epigastrium, small hypodermic injections of morphia, ice pills, sips of very hot water, effervescing mixtures, champagne, one- or two-drop doses of tincture of iodine, are each of them, on occasions, aids in stopping vomiting.

If these measures fail, and if the vomiting is so frequent and so severe that the dose is immediately rejected, and if there is no diarrhœa, it is advisable to clear out the rectum with an injection of warm water and, when the action of this has concluded, to throw up an enema of thirty grains of quinine in three ounces of water with a few drops of acid to aid solution; at the same time, five or ten grains of calomel may be given by the mouth. So soon as the stomach has quieted down, quinine may be given again by the mouth.

Treatment of hyperpyrexia.—Hyperpyrexia must be promptly met by prolonged immersion in the cold bath, rectal injections of iced water, ice bags to the head, etc. At the same time quinine must be injected hypodermically, or into a vein, in full doses, and repeated every three hours until thirty or forty grains have been given. Prompt action in these cases is of the first importance, and may save life. If temperature be kept down for three or four hours the quinine gets time to act on the plasmodia crowding the intracranial vessels; but if temperature be allowed to mount and to remain high the patient is destroyed before the specific has a chance. The cold bath, therefore, is absolutely necessary. In such circumstances, antipyrin and similar antipyretics are worse than useless. Good rules are to prepare to give the cold bath if the axillary temperature reach 106°, and to remove from the bath when rectal temperature has fallen to 102° Fahr.

Treatment of algide and dysenteric attacks.—Algide and dysenteric attacks demand quinine combined with a little opium. If dysenteric symptoms persist, ipecac. or the aperient sulphates in full doses and opium must also be given.

Treatment of hæmoglobinuric fever.—Of all forms of malaria hæmoglobinuric fever is the most resistant to quinine. Some practitioners of experience recommend the exhibition of the drug in heroic doses, giving it every two hours in divided doses to the

extent of 120 grains a day; this they keep up till convalescence is established. On the other hand, hæmoglobinuria may come on while the patient is cinchonised; indeed, some writers of experience—the Plehns and many others—declare that quinine conduces to hæmoglobinuria. After trying it in these cases, and carefully comparing the results of treatment both with and without quinine, these authorities abandoned its use. So long as the hæmoglobinuria continued they treated the case symptomatically, resuming the specific should the case merge into and conclude as a simple intermittent. There can be no doubt that in large doses quinine exercises a certain amount of destructive action on the blood corpuscles, rendering their hæmoglobin unstable. When, therefore, its toxic influence is superadded to that of the malarial poison, it may be that it supplies the little that is required to determine an extensive liberation of hæmoglobin, which, had the quinine been withheld, might not have taken place. Bastianelli (*Annali di Medicina*, Anno ii., Fasc. 11) lays down the following sensible rules with regard to the employment of quinine in hæmoglobinuric fever:—(*a*) If hæmoglobinuria occurs during a malarial paroxysm and parasites are found in the blood, quinine should be given. (*b*) If parasites are not found in the blood, quinine should not be given. (*c*) If quinine has been already given before the hæmoglobinuria has appeared and no parasites are found, its use should be suspended; but if parasites persist it should be continued.

Calomel in large doses—20 to 30 grains—is a favourite remedy for hæmoglobinuric fever. It is systematically used in Africa in these cases. I have heard of it being given there by the teaspoonful. I know of cases which recovered perfectly without a grain of calomel or of quinine.

Quennec has advocated the administration of small doses of *chloroform* in hæmoglobinuric fever. His formula is chloroform 4 grammes, powdered

gum q.s., sweetened water 250 grammes: of this a tablespoonful is given every ten minutes until a certain degree of chloroform intoxication is produced. Thereafter the effect is kept up by enemas of chloral. In twenty-two successive cases he had no death.

Tannic acid is another drug which enjoys a certain reputation in the treatment of malarial fevers which have resisted quinine, and especially in hæmoglobinuric fever. It is given, well diluted, in fifteen-grain doses every two hours for four or five times, the dosing being repeated on the third and sixth days to the extent of two doses each day.

Transfusion of blood has been successfully practised in high degrees of anæmia in some of these cases. *Oxygen* inhalations are indicated, but are rarely practicable.

Precautions.—Patients suffering from or threatened with hæmoglobinuria, or who have had this disease before, on the slightest indication of fever should go to bed at once, keep their skins warm and scrupulously protected from draughts, take plenty of warm fluid, moderate doses—five grains—of quinine every three or four hours (hypodermically by preference), and a large dose of calomel. Those who have once suffered from hæmoglobinuric fever must at all times avoid, above everything, getting wet, or chilled, or over-fatigued, and all other causes of physiological depression. Sitting down to cool off in clothes wet from perspiration or from any other cause is most dangerous. When the urine tends to be suppressed, diuretics must not be given with the idea of stimulating the kidneys. In these circumstances hot fomentations should be applied to the loins, plenty of bland diluents administered, and an exclusive milk diet ordered until all albumen has disappeared from the urine. This is the only rational and safe systematic treatment of the hæmoglobinuric phase of malarial fever. Antipyretics, as antipyrin and phenacetin, are dangerous.

Other drugs in malaria.—During the continuation of a fever I have never seen much, if any,

good from arsenic. The place of arsenic is not as a substitute for quinine during fever but as a blood restorer after fever. I have heard of cases of obstinate ague cured by half-drachm doses of liquor arsenicalis. I have never myself ventured on these heroic doses. I have never seen benefit, in any way approaching that derived from quinine, from methylene blue, carbolic acid, iodine, anarcotine, analgen, phenocol, parthenium, ailanthus, chiretta, eucalyptus, or any of the many drugs which from time to time have, on very limited experience, been recommended in malaria. In those cases, however, in which from some peculiar idiosyncrasy the patient is unable to take quinine, it may be necessary to have recourse to some of these drugs. Methylene blue in doses of two to three grains, and pushed until the urine becomes deeply tinged or signs of kidney irritation appear, enjoys a certain reputation in America and in Germany. Anarcotine was at one time, during a quinine famine, extensively and successfully employed in India; the dose is from one to three grains (*Brit. Med. Journ.*, Aug. 17, 1895). Phenocol hydrochloride, in ten-grain doses, administered five, three, and two hours before the expected paroxysm, has been used with advantage in Italy, and is said to have succeeded in some instances in which quinine had failed. The tannin treatment, already alluded to, might also be tried in obstinate cases where quinine had failed or could not be taken. A grain of capsicum with five grains of quinine is said to succeed sometimes where quinine alone fails. I have given this pill, but how much the capsicum contributed to the cure I cannot say. I cannot say I have ever seen an ordinary uncomplicated ague resist quinine properly given. There can be little doubt, however, that in rare cases it does fail, and that it is more efficient against the benign tertian and the quartan than against the malignant parasites. It does not prevent relapse, however, even in the non-malignant infections.

Treatment of splenic tumour and malarial

cachexia. The enlarged spleen of malarial cachexia is best treated by counter-irritation (linimentum iodi, or ung. hydrarg. biniodid.), and saline aperients, combined with quinine, arsenic, and iron. Hepatic enlargement and abdominal congestion arising from malarial disease of long standing generally derive much benefit from a course of Kissingen or of Carlsbad water; the former preferably if anæmia is marked. Cachectics should leave the malarial centre where they are being poisoned and spend at least one year in Europe. They must be careful to clothe warmly, especially on first entering colder latitudes; to keep lightly employed both in body and mind; to avoid over-fatigue, constipation, exposure to a very hot sun, high winds, rain, to live temperately, and generally to follow the dictates of common sense. A residence in a dry, cool, sunny climate, or a sea voyage, are admirable restoratives in malarial cachexia.

Food and drink in malaria.—The food in malarial fevers ought to be light and principally fluid. Effervescing mixture often helps to clean the tongue and settle the stomach. Lemon decoction (made by boiling for half an hour a sliced lemon in a pint and a half of water, straining, diluting, and sweetening) is a drink that is very much relished in remittents, and may be taken systematically by all malarials with advantage. Fresh lemonade, fresh lime juice water, weak cold tea, and ice water sipped, are all of them much appreciated by these patients. During convalescence the quality of the food should be gradually improved and, if necessary, supplemented by wine or bitter ale.

PROPHYLAXIS.

Drainage, cultivation and flooding.—Experience has shown that much can be done to free a locality of malaria. Drainage and cultivation where the land will repay the expenditure, permanent and complete flooding where it will not and where such flooding is possible, proper paving of unhealthy

towns, a pure water supply, and the filling in of stagnant, swampy pools, these are the leading points to be kept in view in attempting the sanitation of malarious districts. In England, in Holland, in France, in Algeria, in America, and in many other places, enormous tracts of country, which formerly were useless and pestilential, have been rendered healthy and productive by such means Care should be exercised to provide good subsoil drainage in connection with irrigation works, and to avoid interfering with the natural drainage of a district in constructing railways and so forth. To do anything that may raise the level of the subsoil water in malarial districts is most dangerous.

Location of dwelling-houses. — The inhabitants of malarious districts ought to live in villages or towns with well-paved streets and courts, going out to cultivate their fields during the day, but returning to sleep in the town before nightfall. Houses should be placed, if possible, on high and dry situations, a clay soil being avoided. It is unwise in countries such as Africa, where nearly all Europeans suffer from chronic malarial poisoning, to place dwelling houses in exposed situations, or where high winds are apt to produce chills and consequent fever relapses. For the same reason, in elevated situations, houses should be well sheltered by trees or by higher ground. In the neighbourhood of houses the felting of natural grass should, if possible, be preserved, or, if it be disturbed, replaced immediately, or the exposed soil covered with rammed clay or cement. It is unwise to have flower beds or vegetable gardens near bedroom windows, or to allow water from bath-rooms or cook-houses to flow over the ground in the vicinity of the house, or to keep water unchanged in tubs or water-butts for mosquitoes to breed in Pools and puddles of stagnant water should be filled up and turfed. The neighbourhood of swamps is to be avoided. There are many simple precautions of this sort which will occur to every prudent man, and

which, in malarious countries, he should take care to have carried out.

The cultivation of trees and plants.—Much was expected at one time from the cultivation of eucalypti of different species—particularly eucalyptus globulus—as a means of suppressing malaria. Specific virtues were attributed to its balsamic exhalations. These hopes have not been fulfilled in every case; but, undoubtedly, the effect of this rapidly-growing tree in drying the soil, or, perhaps, in keeping away mosquitoes, which are said to object to the peculiar aroma given off by the leaves, is of use in some localities. The same may be said of the cultivation of the sunflower, of the kiri tree, and of other plants. Possibly they too influence insect life, and do good in this way also.

Disturbance of the soil.—The soil must not be disturbed during the sickly season. Workmen so engaged must not sleep near their work.

Native experience to be consulted.—It is unwise to build where the natives say the neighbourhood is unhealthy; natives generally know such places. Neither, if it can possibly be avoided, should a stay be made where the natives are anæmic and have enlarged spleens—a sure indication of an unhealthy district. Water from wells of bad repute, or swamp water, should be avoided, or boiled. We do not know for certain that malaria can be conveyed in water; but it is certain that the natives of many countries think it can; and, as their opinions in such matters are founded on the experience of generations, they should not be ignored.

Other precautions.—If it be true, as is popularly believed, that the liability to the acquisition of malaria is greatest in the evening and early morning, notoriously unhealthy localities should be avoided at these times. In such places sleeping on the ground is dangerous. Bedrooms, therefore, should be situated in an upper storey, and dwelling-rooms be well raised on piles or arches above the ground. Common sense

tells us that campaigns and journeys in malarious districts should be conducted and concluded during the healthy season, if there be one. The possibility of the inoculation of the malaria germ by mosquito bites should not be ignored. Mosquito nets must invariably be used; many travellers attest their value. The body should be covered up during sleep, and every precaution (as fires, eucalyptus boughs, etc.) that circumstances permit should be employed to keep these insects away.

Quinine and arsenic as prophylactics.—A great deal has been written about the prophylactic use of arsenic and quinine in malaria. Opinions are very much divided on the subject. Most deny that arsenic possesses any prophylactic power whatever. Surgeon-Major Duncan, after an exhaustive study of the recorded evidences, and after extensive and carefully conducted experiments made by himself on large bodies of troops, concludes that arsenic has no prophylactic virtue whatever; but that quinine, in a daily dose of three to five grains, lessens the fever admissions by one-half. He therefore strongly advocates the systematic use of the latter drug in all campaigns involving a sojourn in malarious districts. In this he is backed by the opinion of many medical men of experience. Corre, although he admits the prophylactic power of quinine against ordinary malarial fever, says it has no influence in preventing pernicious fevers. Other authorities, on the contrary, state that those who take quinine systematically, though liable to mild fevers to some extent, enjoy immunity from pernicious attacks. On the whole, the evidence is distinctly in favour of the systematic and daily employment of a prophylactic dose of quinine, three to five grains, in malarious districts.

Other prophylactics.—Tea, coffee, and very small doses of alcohol are also decidedly of service; but they should be used in strict moderation, the last being taken only after the work of the day is over,

and Swansea, for example; these little epidemics however, have invariably rapidly died out, and been confined by suitable sanitary precautions to narrow limits.

As stated, in several of the West India islands yellow fever is endemic. It is always to be found in Havana. Formerly the Brazils enjoyed an absolute immunity; but ever since 1849, when yellow fever was introduced for the first time into Bahia by a ship from New Orleans, it has been practically endemic in the large cities. At Rio de Janeiro, although in some years the cases are few, it is never entirely absent. In such places as New Orleans, Charleston, Monte Video, and Buenos Ayres, although now and again epidemics of great severity break out, as a rule several years may pass without its appearing. Some of these epidemic visitations bring a heavy death-bill; thus in New Orleans, in 1853 7,970 people died of yellow fever, in 1867 3,093 died; in Rio, in 1850, it claimed 4,160 victims, in 1852 1,943, and in 1886 1,397. In Havana the annual mortality from this cause ranges from 500 to 1,600 or over.

Ætiology.—*Peculiar limitation.* The reasons for the peculiar geographical limitation of yellow fever are but partially understood. A principal reason undoubtedly is that yellow fever belongs to a somewhat restricted class of diseases which, though communicable, are not directly so through immediate atmospheric conduction from sick to sound; diseases whose germs do not pass quickly from the sick to the healthy, like those of scarlatina or small-pox, but have first, apparently, to undergo extra-corporeally developmental changes that enable them to attack, and to live in, the human body again. Cholera is, perhaps, another such disease; beriberi is probably another; and so, in a sense, is malaria, and all affections whose germs require an intermediate host, or an intermediate nidus. Such diseases, seeing that their propagation demands an additional condition—

the extra-corporeal state or medium—must, *cæteris paribus*, necessarily be more difficult to acquire, must spread more slowly and be more restricted geographically, than the ordinary directly infectious diseases.

Influence of atmospheric temperature.—Another reason for the restriction of the endemic area of yellow fever lies in the fact that either the germ is killed, or the extra-corporeal nidus is in some way rendered unsuitable by low atmospheric temperatures. For its development in epidemic form, yellow fever requires a temperature of over 75° Fahr. It ceases to extend its area when the thermometer sinks below this point, and it stops abruptly as an epidemic when the freezing point is reached; although—as proved by the recurrence of the disease two years in succession in one of the Spanish epidemics, and that without a fresh introduction—the vitality of the germ may not be extinguished and killed outright by frost. Dampness favours yellow fever; it is therefore most prone to occur during the rainy season.

Conditions of soil required.—Further, it is not every spot that affords the extra-corporeal conditions demanded by the germ. It would appear that an admixture of animal matter must enter into the composition of the nidus; decomposing vegetable matter does not suffice.

Unless all of these conditions concur, yellow fever will not establish itself in a locality; consequently, the area of the disease is a restricted one.

A sea coast disease.—The favourite haunts of yellow fever are the sea coast towns, the banks of rivers, and flat delta country. Rarely does it pass far inland, or ascend high ground. Still, there are exceptions to these general rules; for it has been found, on rare occasions, far inland, and at a considerable elevation (Newcastle, Jamaica, 3,000–4,000 feet; Cuzco, Peru, 9,000–10,000 feet). Villages are rarely affected; nor does the disease readily spread if introduced into rural localities.

A ship disease.—As in the case of beriberi, the

somewhat limited conditions found on board ship supply the requirements demanded by the germ of yellow fever. Ship epidemics are common occurrences. Its ideal haunt, however, is the low-lying, hot, squalid districts in the neighbourhood of the wharfs and docks of large seaport towns.

A place disease. Yellow fever, therefore, is a place disease like malaria or beriberi. If the patient is removed to a hitherto unaffected spot his attendants and neighbours do not contract the disease, unless the spot itself first become infected. The occurrence of this place infection will depend on whether the particular locality affords a suitable nidus for the germs which escape from, or are brought by, the patient. If the locality supplies these conditions, then, for the time being, the disease spreads and becomes epidemic; if the locality does not supply these conditions, then the disease does not spread.

In Havana, although the harbour is narrow, the crews of ships anchored in mid-harbour do not contract yellow fever unless they go on shore, or unless the ship itself becomes infected by fomites conveyed from the shore. But if the same ship moor alongside a wharf the crew may be at once attacked. It is safe, therefore, to visit a yellow fever patient if he is lodged outside the endemic area; but it is never safe for the susceptible to visit the endemic area, whether they come into direct contact with the sick or not.

Nott has pointed out that yellow fever occurring in a many storeyed building attacks especially those living on the ground floor It picks out particular localities, houses, and streets, apparently in the most capricious way.

Immunity acquired by prolonged residence or by a previous attack.—A curious fact about yellow fever is that the natives of, and those who have lived for a long time in, the endemic area are practically exempt from the disease; or, if they are attacked, the disease is usually of a very mild type. It is also said that if the native quits the endemic

area his immunity decreases in proportion to the length of time he remains away; so that after long absence, on his return to the endemic area, he may be attacked just as an ordinary visitor might be. Further, those who enter the endemic area for the first time are the most susceptible, the susceptibility decreasing with length of residence. It is probable, therefore, that at such places as Rio the endemicity of the disease is kept up by the continual stream of foreign and, therefore, susceptible visitors. One attack of yellow fever is almost invariably protective against a recurrence.

Race as influencing susceptibility. — Another curious fact is that the negro is little liable to yellow fever, and that when he gets it the attack is usually mild. The yellow-skinned races are more susceptible than the negro, but less so than the European. It is also said that the susceptibility of the European increases in proportion to the height of the latitude of his native place; that is, a Norwegian will be more susceptible than a Frenchman, and a Frenchman more than an Italian or Spaniard.

Incubation period.—The incubation period of yellow fever rarely exceeds four or five days; it may be much shorter—under twenty-four hours. The limits, according to Bérenger-Féraud, are one to fifteen days in the temperate zones, one to thirty days in the tropics. Occasionally it happens that the disease breaks out in a ship after she has been several weeks at sea, having had no communication with the land or with another ship in the meantime. It must not, however, be inferred from this that the incubation period is to be reckoned in weeks. The ship itself, the cargo, or timbers, or the clothes of the crew were infected in port; but the crew had not, until long afterwards, caught the infection from the particular part of the ship in which the virus had been brewing or latent. The ship was infected for weeks, but not the crew. Exactly the same thing happens in the case of ship beriberi.

Symptoms.—There is the same variety in the initial symptoms of yellow fever as in the other specific fevers. There may be sudden rigor supervening in the midst of apparent health; there may be only slight chills; or there may be a period of premonitory malaise leading up to the more pronounced symptoms. When fairly started, the procession of events is rapid.

Roughly speaking, and provided there are no complications, an attack of yellow fever is divisible into three stages: 1. The initial fever; 2, "the period of calm," as it is called; and 3, in severe cases, the period of reaction.

The initial fever lasts usually from three to four days. The maximum temperature is generally attained within the first twenty-four hours, or by the second day, and, in a case of medium severity, may rise to about 103° to 104° Fahr. During the three or four succeeding days the mercury slowly sinks to 98° or 99° Fahr., the diurnal fluctuations being seldom more than half to one degree. It occasionally happens that high temperature is maintained for two or three days, and also that the maximum is not attained till the third day; but, as a rule, the thermometer behaves as described, the maximum being reached within a few hours of the declaration of the disease.

With, or soon after, the initial chill or rigor severe headache sets in, and is generally a prominent feature. For the most part the pain is concentrated about the forehead, in the circumorbital region, and in the eyeballs themselves. In many cases it is associated with intolerance of light.

Loin pain is another very distressing symptom; it may amount to positive agony. The legs, too, ache excessively—particularly the calves, knees, and ankles; they feel as if broken.

The face is flushed and swollen; the eyes are shining, injected, and ferrety, the skin is dry; and what with pain and febrile distress, the patient rapidly

passes into a very miserable condition. He is restless, and continually tossing about.

At first the pulse ranges from 100 to 120 per minute, and is full and strong; but, as the disease progresses, it loses its sthenic character, gradually falling in force and frequency until at the "period of calm" it becomes remarkably slow and compressible, beating perhaps only thirty or forty times per minute.

At the outset the tongue is not very dirty, but it soon acquires a white coating on the dorsum, the edges remaining clean. It is not so swollen and flabby as in malarial fever; on the contrary, it is often small and pointed throughout the disease. This is regarded as an important diagnostic mark; taken along with the progressive diminution in the strength and frequency of the pulse, and the peculiar behaviour of the temperature, it is nearly conclusive as to the disease being yellow fever. Later, the tongue dries, and, at the same time, thirst becomes intolerable. The palate is congested and swollen; the gums may also swell and bleed.

As mentioned, the features at first are flushed and swollen. This congested appearance tends to subside, so that by the time the asthenic stage is reached, the features may have become shrunken and small, the eye sunken, and the eyelids may have become discoloured by ecchymoses.

In some cases the skin is hot and dry throughout; in others it may be bedewed with perspiration from time to time; or the sweating may be constant, especially if collapse occurs.

By the third day the scleræ assume a yellowish tinge, and very often the skin acquires the yellow colour from which the disease derives its name. It must be understood, however, that it is not every case that presents this colour of skin; in some it is entirely absent. The yellow tinge generally shows about the end of the first stage, deepening in intensity as the case advances, and remaining apparent for a considerable time after convalescence has become

established. It ranges in depth from a light saffron tint to a deep mahogany brown In fatal cases it is always present; not necessarily during life, but invariably after death. The skin is said to emit a peculiar odour like gun washings, or, as Jackson puts it, like the smell of a fish market.

Petechial, erythematous, papular and other eruptions may show themselves in different cases; but in yellow fever there is no characteristic eruption.

An important feature, from the diagnostic as well as from the prognostic point of view, is the appearance, in some cases almost from the outset of the disease, of albumin in the urine, together with a tendency to suppression. In mild cases these features may be little marked; but in severe cases, particularly during the stage of depression, the urine may fall to a few ounces, and be loaded with albumin to the extent of one-half or even two-thirds. The more pronounced these symptoms, the graver is the prognosis. Urea and uric acid are very much diminished, the former in severe cases falling to 1·5 gramme to the litre. The urine is almost invariably acid. Bile pigments show themselves towards the end of the disease, their appearance is regarded as a favourable omen. Hæmorrhage from kidneys or urinary tract is not uncommon.

Delirium may occur, but is not an invariable feature. Usually, after the initial stage of restlessness and acute suffering, the patient becomes torpid, and perhaps taciturn. In bad cases coma, subsultus, etc., may gradually supervene, the temperature rising as death approaches and even after death.

At the outset the bowels are confined. In the second stage, diarrhœa, perhaps of black material resembling the vomit, may supervene; or there may be actual hæmorrhage of bright red blood from the bowel.

The well-known *black vomit* — always a grave symptom, but fortunately not by any means an invariable one forms one of the most striking features

of this disease In the earlier stages of the fever vomiting of bilious matters is a common occurrence. This may subside, or, after a time, give place to a coffee-ground vomit which gradually deepens in colour until it becomes uniformly black. On microscopic examination the vomited material is found to consist of broken-down blood corpuscles and altered hæmoglobin suspended in a yellowish mucoid fluid. This material is, doubtless, in the main derived from blood transuded through the walls of the capillaries of the mucous membrane of the stomach. It is intensely acid. Though the black vomit may not always be seen in fatal cases during life, this characteristic material is invariably found in the stomach on *post-mortem* examination.

Sometimes pure blood is thrown up from the stomach; similar passive hæmorrhages may take place from almost any part of the body—from eyes, ears, nose, mouth, bladder, uterus, and so on.

Death may occur during the early acute stage, being preceded by a rapid rise of temperature.

In mild cases the "period of calm," which sets in after the subsidence of the initial fever, may last for several days before convalescence is established. In such, recovery once begun is usually very rapid; in a week from the beginning of the disease the patient may be about again. In severe cases, however, the period of calm is followed by a third stage, the stage of reaction, in which the temperature again rises, though not to so high a point as in the initial fever, and a sort of remitting fever of an adynamic type keeps on for several days or weeks. This secondary fever is prolonged more especially if there is any complication such as abscess, boils, parotitis, buboes, hepatitis, and so forth. The icterus is now very pronounced; black vomit may recur or appear for the first time; perhaps a profuse diarrhœa ends in collapse; or the urine may be suppressed, stupor, coma, and other nervous symptoms ensuing, and very often ending in death. In other instances the

secondary fever terminates in a crisis of sweating and a prolonged convalescence.

Relapse may occur at any time up to two or three weeks after the subsidence of the initial fever. It is specially prone to occur if the patient has been guilty of any dietetic imprudence during the period of calm—a period at which the appetite may return to some extent. Relapses are very dangerous.

Prognosis and mortality. — The prognosis in yellow fever is good if the temperature during the initial fever does not exceed 103° to 105 Fahr. It is better for women (although if pregnant, abortion is almost invariable) and children than for men; better for old residents than for newcomers; worst of all for the intemperate. According to a table of 269 carefully-observed cases given by Sternberg, there were no deaths in 44 cases in which the temperature did not rise over 103°; *per contra*, in 22 cases in which the thermometer rose over 106° there were no recoveries. Of 36 in whom the temperature rose to between 105° and 106°, 22 died; of 80 with maximum temperatures between 104° and 105°, 24 died; and of 87 in whom it ranged between 103° and 104°, only 6 died. The mean mortality in the whole 269 cases was 27·7 per cent. This may be taken as a fairly representative mortality in yellow fever among the unacclimatised, something between twenty-five and thirty per cent., although in some epidemics it has risen as high as fifty or even eighty per cent. of those attacked. Among the permanent inhabitants of the endemic districts the case mortality is very much lower—seven to ten per cent. During epidemics abortive and ambulatory cases occur; in these, icterus and other characteristic symptoms are often absent. Such cases may be hard to diagnose from febricula or mild malarial attacks. In them the mortality is nil. Some epidemics are particularly mild. In the same epidemic the cases may vary in severity from time to time.

Pathological anatomy.—Depending probably on hæmoglobin diffused in the liquor sanguinis and

tissues, and not on biliary pigment, the yellow colour of the skin is most marked in the dependent parts of the cadaver, especially in those parts which are subjected to pressure. Petechiæ are common in the skin; more considerable extravasations of blood may be found in the muscles. The brain, and contents of the skull generally, are hyperæmic. The brain tissue may be studded with minute hæmorrhagic effusions; like the other tissues of the body, it is stained a lighter or deeper yellow. The blood in the vessels of the general circulation is not firmly coagulated. The blood-corpuscles appear to be normal, although there can be little doubt that there is in this disease a liberation of hæmoglobin, arising, possibly, from destruction of a proportion of the corpuscles. An important fact, as explaining the liability to passive hæmorrhages, is the existence of a fatty degeneration of the capillaries and smaller blood-vessels. The stomach, as stated, always contains more or less black material, such as may have been vomited during life. Here and there in its mucous membrane are arborescent patches of congestion and ecchymoses. Observers are not agreed as to the nature of this congestion, as to whether it is passive or inflammatory. Sternberg says there is evidence in the increase of leucocytes in the submucosa of a slight inflammatory action. The small intestine may contain a dark acid material similar to that in the stomach, and doubtless coming from the same source. Like that of the stomach, the mucous membrane of the intestine shows patchy arborescent injection.

As compared with other fevers, the liver is characteristically affected in yellow fever. As a rule, if death have occurred at the later stages, it is somewhat exsanguine, friable, and presents a yellowish colour from profound fatty changes in the cells. Occasionally, though rarely, it may be hyperæmic and dark. Here and there throughout the gland the cells—particularly those about the periphery of the lobules—on microscopical examination are found

to contain globules and grains of fat. The nuclei in some instances, as well as the protoplasm of the cells, show fatty changes. This profound fatty degeneration of the liver cells is well marked in the great majority of cases.

The kidneys are affected with parenchymatous nephritis. Hæmorrhagic foci under the capsule and in the cortex are common. The renal epithelium shows cloudy swelling passing on to fatty degeneration and desquamation. The tubules, here and there, are filled with infarcts, either of an albuminoid material or of *débris* of desquamated epithelium, corresponding with the numerous casts which can be discovered in the albuminous urine.

The germ.—A great many attempts have been made to discover the germ or virus of yellow fever, and a corresponding variety of organisms have been described. One of the best known and, at one time, most talked about, was the cryptococcus xanthogenicus which Dr Freire, of Brazil, proclaimed as the true cause. He even went the length of practising protective inoculations by cultures of this organism, prepared on the Pasteurian system of attenuation.

Dr. Finlay, of Havana, who regards the mosquito as a principal agent in the diffusion of the germ of yellow fever, claims for another organism—the tetragonus febris flava—the distinction of being the true virus. He has practised inoculations by the bites of mosquitoes previously fed on yellow fever patients, and claims that as the virulence of an attack depends on the number of infected mosquitoes biting the inoculated, by reducing the number of bites a mild yet protective attack can be thereby harmlessly induced.

At the instigation of the Government of the United States, these and other organisms have been rigidly investigated by Sternberg, whose standing as a bacteriologist, and whose judicial cast of mind, eminently qualify him for forming a trustworthy judgment. His verdict on these, and many similar

organisms for which pathogenic claims have been advanced, is unfavourable.

Sanarelli (*British Medical Journal*, July 3, 1897), whose record as a bacteriologist gives great weight to his statements, claims to have found in a highly pleiomorphic bacterium, which he has named *bacillus icteroides*, the germ of yellow fever. This bacillus is present in small numbers, and almost invariably associated with streptococci, staphylococci, and bacillus coli, in the blood and tissues, especially the liver. It is not found in the contents of the alimentary canal. It is easily stained and readily cultivated in the usual media, growing characteristically. Injected into animals it proves exceedingly toxic, giving rise to symptoms and lesions resembling those of yellow fever. Filtered cultures injected into five men produced typical yellow fever, including hæmorrhage, icterus, anuria, delirium, collapse, and, as steatosis of the liver and nephritis are mentioned, conditions which can only be ascertained *post-mortem*, presumably death. Important practical points in the biology of the bacillus are : It strongly resists drying ; it dies in water at 60° C. ; it is killed by seven hours' exposure to the sun ; it lives a long time in sea water ; the development of moulds on a culture favours the bacillus. Doubtless these statements will be rigidly tested ; if confirmed, we may see ere long important practical results.

Diagnosis. — The subject of the diagnosis of yellow fever has already been treated of under "Malaria" (pp. 107–8), to which the reader is referred. Practically, the only two diseases with which yellow fever may be confounded are bilious remittent and bilious hæmoglobinuric fever.

Treatment.—Formerly, a much more active treament than that in vogue at the present day was the fashion for yellow fever. It is now recognised that, as with most specific fevers, the treatment is more a matter of nursing than of drugs.

Experience has shown that a smart purgative at

the very outset of the disease is beneficial. With many castor oil is the favourite drug, but, to be of service, it has to be given in very large doses—two to four ounces. Others use calomel, or calomel combined with quinine—twenty grains of each. Others, again, prefer a saline. The purgative, whichever be selected, must not be repeated, or, for that matter, given at all if the patient is not seen until after the second day of the disease.

Hot mustard pediluvia, frequently repeated during the first twenty-four hours, the patient and bath being enveloped in a blanket, are in constant use in yellow fever epidemics. They are said to relieve the cerebral congestion and the intense headache. Very hot baths, with subsequent blanketing and sinapisms to the epigastrium, are also said to have a similarly favourable influence on the congestion of the stomach, which is, undoubtedly, another constant feature of the disease. For high fever antipyretic drugs, cold baths, iced injections, cold sponging and the like may be carefully employed. In view of the asthenic nature of the disease, the less depressing measures should be preferred.

Vomiting may be treated with sinapisms and ice pills, or with small doses of cocaine. Morphia is dangerous, and must be avoided. For black vomit, frequently repeated doses of perchloride of iron, ergotine injections, acetate of lead, and other styptics have been recommended. For restlessness, phenacetin or antipyrin is used. When the skin is dry, the urine scanty, and the loins ache excessively, Sternberg recommends pilocarpine.

After the fourth or fifth day the flagging circulation demands stimulants of some sort. Iced champagne, hock, or teaspoonful doses of brandy given every half hour, may tide the patient over the period of collapse. Great care, however, should be exercised in the use of these things; if they seem to increase the vomiting and the irritability of stomach, they must be stopped at once.

The feeding is an important matter. So long as there is fever the patient has no appetite; during this time—that is, for the first two or three days—he is better without food. When the fever subsides appetite may return, and a craving for nourishment become more or less urgent; the greatest care, however, must be exercised about gratifying this untimely appetite. Only the very blandest of foods, and these only in very small quantities, should be allowed—spoonfuls of iced milk or chicken tea. Gradually the quantities may be increased; but, even when convalescence is established, solid food must be partaken of very sparingly, and it must be of the simplest and most digestible description. Indiscretion in eating is a fruitful cause of relapse in yellow fever; and it must be borne in mind that in this disease relapse is exceedingly dangerous. Nutrition may be aided by nutrient enemata.

The Sternberg treatment.—Sternberg has introduced a system of treatment by alkalies which promises well. It is directed principally to counteracting the hyperacidity of the gastric and intestinal contents—always a marked feature in yellow fever. His prescription is 150 grains of sodium bicarbonate and one-third of a grain of mercury perchloride in a quart of water; of this an ounce and a half is given every hour. This, he claims, not only neutralises the acidity of the intestinal contents but increases the flow of urine, the perchloride of mercury tending to check fermentative change in the alimentary canal. Of 301 whites treated in this way only 7·3 per cent. died, and of seventy-two blacks all recovered. Other encouraging figures have been adduced as to the efficacy of this line of treatment, which is certainly deserving of further and more extended trial.

Prophylaxis.—During epidemic visitations, or during exacerbations of endemic yellow fever, the unacclimatised should, if possible, immediately quit the implicated zone. Above all, the slums and low-lying districts of the town should be shunned; these

places should not even be visited; or, if visits have to be made to them, these visits should be as brief as possible and not made during the night. The susceptible should avoid sleeping in the lower storeys of their houses, and pay great attention to their general health, carefully avoiding all causes of physiological depression or disturbance. Sailors must not be allowed on shore.

In every country subject to visitations of this disease the sanitary conditions of the towns should be most carefully attended to. Experience has shown that nothing invites yellow fever so surely as filth and overcrowding. Ships should not be allowed to clear from infected ports, nor to enter non-infected ports, during the warm season, without adequate inspection. If yellow fever is found on board, the cases should be isolated in a proper quarantine hospital, the ship thoroughly disinfected, and the crew prevented for at least five days from communicating with the shore, or until every risk of conveying infection has passed away. The destruction of all fomites is imperative. Clothes, books, and so forth must be rigidly and thoroughly disinfected, and every feasible means employed to prevent the formation of fresh foci of disease around the patients. In the event of the disease appearing in a locality which is not habitually a yellow fever centre, the most economical plan of dealing with the threatened danger is for the authorities promptly to remove the entire population of the neighbourhood, with the exception of the insusceptible and those in attendance on the sick, and to place the deported population before dispersion in a ten days' quarantine camp. Meanwhile, the infected area must be rigidly isolated. In this way it has been found possible to prevent the spread of the disease.

In the event of yellow fever breaking out in the crew of a man-of-war, the cases, if possible, should be sent ashore, and the ship hurried north or

south into cold weather, every sanitary precaution being employed meanwhile.

There is an important matter, in connection with this disease, which in the near future ought to be made a subject for international consideration, and that is the prevention of the spread of yellow fever to Asia, the Eastern Archipelago, Polynesia, and East Africa. It has spread in the past to Europe; this is a comparatively unimportant matter, as the climatic and hygienic conditions in that continent are not favourable to the extension of the disease. It is otherwise, it is to be feared, in this respect with Asia. Fortunately, yellow fever, so far as known, has never appeared in the crowded, filthy cities of the East; but should it ever be introduced, the favourable climatic conditions and the surpassing filth everywhere present there will enable it to spread like wildfire. The probable reason of its non-introduction into Asia is that the trade route from the West Indies to China and India has hitherto not been a direct one, but has passed by a long circuit either to the north or to the south. When a Central American canal has been constructed, as it most likely will be, and at no distant date, then there will be direct and rapid communication between the present yellow fever centres and Asia. With this more direct and more rapid communication there will arise a corresponding risk of spreading yellow fever into a huge section of tropical humanity which has hitherto enjoyed exemption from one of the deadliest diseases afflicting mankind. Let us hope that before the Central American canal is opened this important matter will not be lost sight of; and that due care will be exercised that America does not reciprocate the introduction of cholera from Asia by a gift of yellow fever.

CHAPTER VIII.

BUBONIC PLAGUE.

Definition.—Plague is a specific, inoculable, and otherwise communicable epidemic disease common to man and many of the lower animals. It is characterised by fever, the development of buboes, a rapid course, a very high mortality, and the presence of a specific bacterium in the lymphatic glands, viscera, and blood.

Geographical distribution. — Though not necessarily confined to such, in modern times plague, like leprosy, has become practically a disease of warm climates. The hygienic conditions which advancing civilisation has brought in its train have forced back these two diseases from Europe where, at one time, they were even more prevalent than they are in their tropical and subtropical haunts at the present day. They are typical examples of that large group of acute and chronic germ diseases whose spread depends on social and hygienic, rather than on climatic, conditions, and more especially on filth and overcrowding; conditions which nowadays are found, to an extent and an intensity sufficient to ensure the endemic prevalence or epidemic extension of these diseases, only in warm countries.

It is difficult to say what the *pestis* of the ancients may have been. Probably in many instances it was bubonic plague; doubtless the term was sometimes applied to other epidemic sicknesses attended with a large mortality.

The descriptions which have come down to us of these old-world epidemics are too vague for recognition. According to Hirsch, the first recognisable

description of what is now understood by plague refers to its occurrence in Libya, Egypt, and Syria about the end of the third and the beginning of the second century before the Christian era. The next authentic account, and the first as regards Europe, refers to the great epidemic known as the plague of Justinian, which, in A.D. 542, starting from Egypt, spread to Europe and all over the Roman Empire; and which, lasting for fifty or sixty years, wrought the most frightful devastation wherever it reached, depopulating the towns and turning the country into a desert. From that time until 1841, when plague appeared for the last time in Constantinople, it recurred again and again in different parts of Europe, though latterly only in the south-eastern parts of the continent and in areas becoming gradually more circumscribed. In 1878–79 a small epidemic, which speedily died out, broke out in the Russian province of Astrakhan. With the latter exception, Europe has long enjoyed exemption from this worst of epidemic diseases. The plague visited England for the last time in 1664–79, when, in 1664–65, upwards of 70,000 perished of the 460,000 inhabitants of the London of that day.

Egypt, in former times the favourite haunt of the disease, has been exempt since 1844, although several epidemics have since that date occurred in its neighbourhood—in Tripoli (Benghasi) in 1856, in 1859, and in 1874; and on the Red Sea coast of Arabia (Assir) from 1853 to the present time. It is said to be endemic in Uganda. Epidemics have occurred in Mesopotamia (last in 1892), in Turkestan (last in 1892), in India, and in China.

In India there have been many outbreaks during the current century, but they have been of a localised rather than of a general character. One, beginning in Cutch in 1815, spread to Scinde and Gujerat, and continued to 1821. Epidemics have also occurred in Kumaon and Gharval on the southern slopes of the Himalayas in 1824, 1834–37, 1846–53, 1876, and 1884; also at Hansi in Delhi, 1828–29. In 1836

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than those found in the glands, and, according to Aoyama, are stainable by Gram's method, whereas the bacilli of the glands are larger and are decolourised by this process.

Culture characters.—When sown on blood serum and kept at body temperature, in from twenty-four to forty-eight hours an abundant, moist, yellowish-grey growth is formed without liquefaction of the culture medium. On agar, but better on glycerine agar, the growths have a greyish white appearance. In agar plate cultures they show a bluish translucence, the individual colonies being circular, with slightly irregular contours and a moist surface. Young colonies are glass-like, but older colonies are thick at the centre and more opaque. Stab cultures show after one or two days a fine dust-like line of growth. According to Yersin, when sown on gelatine the bacillus gives rise to white transparent colonies which, when examined in reflected light, present iridescent borders. In bouillon the cultures present a characteristic appearance, the liquid remains clear whilst a granular deposit takes place on the sides and bottom of the tube. Examined with the microscope these various cultures show chains of a short bacillus, presenting here and there large bulbous swellings. In gelatine the bacilli sometimes form fine threads, sometimes thick bundles made up of many laterally agglomerated bacteria.

The most favourable temperature for cultures is from 36° Cent. to 39° Cent.

The bacillus, according to Kitasato, does not form spores.

Experimental plague.—Intentional and unintentional experiments have proved or, rather, made probable, the inoculability of plague in man. Whyte, in 1802, communicated the disease to himself and died of it. At Cairo, in 1835, two condemned criminals were inoculated from the blood of plague patients; they contracted the disease but recovered. The value of these experiments, as proving inoculability,

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numerous bacilli in the lymphatic glands, blood, spleen, and other viscera. Guinea-pigs die in from two to five days after inoculation, mice in from one to three days. Sheep and swine are feebly, if at all, susceptible (Lowson).

In the case of the guinea-pig, within a few hours of the introduction of the virus a considerable amount of œdema is already apparent around the puncture, and the adjacent gland is perceptibly swollen. At the end of twenty-four hours the animal is very ill; its coat is rough and staring, and it refuses food. Presently it falls on its side and becomes convulsed, one fit following another with increasing frequency as death approaches. If the body is opened immediately after death a rosy red sanguineous œdema is found at the point of inoculation, and hæmorrhagic inflammatory effusions around the nearest lymphatic gland, which is much swollen and full of bacilli. The intestines are hyperæmic; the adrenals, kidneys, and liver are red and swollen. The much enlarged spleen frequently presents an eruption of small whitish granulations resembling in

* The pus from a bubo is not always infective. Inoculations made with such may fail. Apparently the bacteria of suppuration may kill the bacillus pestis.

appearance miliary tubercles. All the organs, and even any serous fluid that may be present in peritoneum or pleura, will be found to contain plague bacilli. In the blood, besides those free in the liquor sanguinis, bacilli are to be found in the mononuclear though not, it is said, in the polynuclear leucocytes.

The disease is readily communicable to the lower animals from cultures.

Intensification and attenuation of virus.—There can be no question that, both by artificial means and in a natural way, the virulence of the bacillus of plague is susceptible of modification. It has been remarked on two occasions, in Russia and in Persia, that outbreaks of plague were preceded by a sporadic, or epidemic febrile, sometimes afebrile, affection in the course of which the lymphatic glands became enlarged and perhaps suppurated. Cases which may have been of this nature (although this is disputed), and in which a bacteriological examination proved that a cocco-bacillus was present in the blood and enlarged glands, are recorded by Drs. Cobb and Simpson (*Indian Med. Gaz.*, Nov. 1896). It is further known that in some instances the virulence and case mortality of a plague epidemic show a tendency to decrease, the early cases being the most frequently and most rapidly fatal. These two facts seem to indicate that under certain unknown natural conditions the virus tends to acquire increased potency, whilst in other circumstances its virulence tends to diminish.

This conjecture is countenanced by the results of certain experiments on animals. It has been experimentally shown that by passing the virus by inoculation from one guinea-pig to another the rate of its action becomes accelerated. On the other hand Yersin remarks that, although it is difficult to start a gelatine-peptone cultivation, nevertheless, when obtained, such a cultivation—at all events, certain parts of such a cultivation will be found to be quite as lethal as virus derived directly from a bubo. He

further observed that in such cultures a certain proportion of the colonies developed more rapidly than others; that if inoculation were made from these more rapidly developed colonies, their virulence is found to be diminished, and that if these rapidly growing cultures are frequently repeated, in the long run they cease to be fatal to guinea-pigs, although they may still prove fatal to white mice. During the height of the Hong Kong epidemic the same observer asserted that he found in the soil forming the floor of plague-haunted houses, four to five centimetres below the surface, a bacterium with all the morphological, staining, and culture properties of the plague bacillus, but which was devoid of virulence. This, which, if confirmed, would be an important observation from the ætiological standpoint, has been strenuously denied.

These various natural and experimental data indicate a very pronounced tendency to mutability as regards virulence on the part of the plague bacillus; a disposition which, in the future, may very well be turned to important practical account.

Feeding experiments. Rats or mice fed on cultures, or on fragments of the liver or spleen of animals dead of plague, acquire the disease and generally die with the characteristic symptoms, lesions, and bacilli.

Experiment on contagion.—Yersin placed in the same cage healthy and inoculated mice. The inoculated mice died first, but afterwards the originally healthy and uninoculated mice also succumbed; proving that plague is not only inoculable but that it is also communicable either through the atmosphere or by contact.

Conditions favouring naturally acquired plague.—The most potent circumstances which predispose to the epidemic outbreak of plague are extreme filth and overcrowding. In such circumstances the virus, once introduced, tends to spread. These conditions, however, are not all-sufficient; for even in the filthiest

and most crowded Oriental towns, and without any apparent alteration in the habits or circumstances of the population, the disease, after having become epidemic, dies out spontaneously. It may be difficult to indicate the exact way or ways in which filth and overcrowding operate, but certain it is, as experience has shown, that in sanitary hygienic conditions plague does not spread even if introduced, and that in opposite conditions it may for a time spread like wildfire.

Filth and overcrowding imply close proximity of the sick and the healthy; an atmosphere saturated with the emanations of the sick; a lowered tone of the general health; abundant saturation of soil and surrounding media with animal refuse, fitting them as a nidus for what might be termed natural culture of the germ; abundance of body vermin of all kinds, abundance of other vermin, such as rats and mice, which serve as multipliers of the virus; carelessness about personal cleanliness, about wounds of the hands and feet, about clothing, and about food, dishes, and water. One can understand how in such circumstances the germ has opportunities to multiply and spread.

Plague, though "catching," is not nearly so infectious as are scarlet fever, measles, small-pox, or even typhus. Medical men, and even nurses, in clean airy hospitals rarely acquire the disease, provided they have no open wounds and do not remain too long in close proximity to their patients. In cities the cleanly districts are generally spared. This was well exemplified in the late epidemics at Canton and Hong Kong where the airy, cleanly European quarters and the relatively clean, well-ventilated boat population were practically exempt; whilst the disease ran riot in the adjoining filthy, overcrowded native houses only a few yards away

The fact that plague can be communicated to the lower animals by feeding them on the tissues of plague patients and on cultures of the specific bacillus, suggests that the disease may be conveyed to man in food or drink. Kitasato has found the

bacillus in the intestinal contents of patients. Water or food contaminated with sewage or fæcal matter may, therefore, be regarded as a possible medium of infection.

It would appear that a certain degree of concentration of virus, such as we may assume to exist in direct inoculation into wounds, or a prolonged exposure to concentrated aerially borne germs, is necessary for successful infection. Germs do not penetrate the unbroken epidermis, as proved by the impunity with which *post-mortem* examinations are made; but it seems not improbable that in a considerable proportion of instances the plague germ is introduced through trifling wounds of the feet. It is conceivable that such germs as may be lying about on the ground, deposited there in the discharges of sick human beings or of plague-stricken animals, or perhaps growing there in natural culture, may be picked up in this way. The frequency with which the primary bubo, as will be pointed out, is located in the deep femoral glands suggests this. One can understand, too, how lice, fleas, bugs, and perhaps flies might act as carriers of the virus from person to person, inserting it with their bites. Yersin found that the flies in his Hong Kong plague laboratory died in great numbers, their bodies being crowded with the specific bacillus; he injected bouillon containing a trituration of one of these flies into a guinea-pig, and the animal presently died with all the signs of plague. Sablonowski, who in 1884 in a measure anticipated the discovery of the bacillus by Kitasato and Yersin, remarked that during the Mesopotamian epidemic of that year a certain species of fly appeared and disappeared concurrently with the plague, he considered that this insect was an active agent in spreading the disease.

Plague among rats, etc.—Many observers have remarked the great mortality among rats and other animals which sometimes precedes and accompanies outbreaks of plague in man. Writing about the

mortality among rats during the recent Canton epidemic, Rennie (*Chinese Imp. Mar. Customs Gaz. Med. Rep.*, No. 48) remarks that the Chinese regarded this unusual and striking occurrence as a sure indication of an extension of the epidemic. From districts of the city where the plague had been raging for some time the rats entirely disappeared, whilst they kept on dying in other quarters to which the disease afterwards spread. The rats, he says, would come out of their holes, in broad daylight even, and tumble about in a dazed condition and die. Certain Chinese officials took steps to have all dead rats collected; in a very short time one officer collected upwards of 22,000.

Rocher (*Chinese Imp. Cust. Gaz. Med. Rep.*, No. 15) states that in Yunnan the mortality among the rats is particularly noticeable. Other animals also die he says, oxen, sheep, deer, pigs, and dogs are all attacked at times, the dog less severely and frequently than the others.

Pringle (*Brit. Med. Jour.*, 8th Aug., 1896) says that in the Shuiwal, Himalayas, where in 1864 plague was epidemic, the rats quitted the various villages in anticipation of the advent of the disease; and that the people, taught by experience, on seeing this exodus recognised it as a warning.

These facts with regard to plague in the lower animals throw important light on one of the ways in which the disease is spread; and it seems to me that they have to be reckoned with in the future, more than they have been in the past, in devising schemes of quarantine, and in attempts at stamping out the disease in already infected localities. It seems to me that the wholesale destruction of domestic vermin should go hand in hand with the isolation of plague-stricken patients.

Age, sex, and occupation have very little influence in plague. The youngest children are susceptible; old age seems to be to a certain extent protective, the disease being rarer after fifty than during adolescence.

Women, doubtless on account of their remaining much indoors in the tainted surroundings, are relatively more frequently attacked than men.

Geological constitution of soil appears to have no direct influence on plague.

Atmospheric temperatures, if very high or very low, seem to have a repressing effect Thus, as a rule, epidemics in Egypt and Mesopotamia declined during the height of the very hot and dry summer, and in Europe during the extreme cold of winter. On the other hand, plague, on more than one occasion, has flourished during a Russian winter; and also, as in Hong Kong recently, during the heat of a tropical summer On the whole, the evidence points to moderate temperatures combined with a certain degree of dampness as being the principal atmospheric conditions favouring epidemic outbreaks.

Elevation, as regards sea-level, does not directly affect the general distribution of the disease. Indeed, mountain tribes, probably on account of their poverty and squalor, are peculiarly liable to epidemics. In houses the ground floor is more dangerous than the upper storeys.

The *extension of plague epidemics* is peculiar, and in many respects resembles that of cholera. Sometimes it spreads rapidly from point to point; more generally it creeps slowly from one village to another, from one street or one house to another. Sometimes it skips a house, a village, or a district to appear there later. Particular houses, and even particular floors of houses (Lowson), may be infected, whilst those in the neighbourhood are free from the disease. Manifestly its extension depends more on place infection than on direct transmission from person to person.

Symptoms.—*Incubation period.*—Symptoms of plague begin to show themselves after an incubation period of from two to eight days. It is said that in certain very rare instances the incubation period may extend to as much as fifteen days. It is also

said that in highly malignant epidemics the disease may declare itself within three or four hours from the time of exposure to infection.

Prodromal stage. — In a certain but small proportion of cases there is a prodromal stage characterised by physical and mental depression, anorexia, aching of the limbs, feelings of chilliness, giddiness, palpitations, and sometimes dull pains in the groin at the seat of the future bubo.

Stage of invasion. — Usually, however, the disease sets in somewhat suddenly with fever, extreme lassitude, frontal or, more rarely, occipital headache, aching of the limbs, vertigo, drowsiness or perhaps wakefulness, troubled dreams. Rigor is rarely a marked feature; more often the disease is heralded by unimportant feelings of chilliness. The face quickly acquires a peculiar expression, the features being drawn and haggard, the eyes bloodshot, sunken and staring, the pupils probably dilated, sometimes the face wears an expression of fear or horror The patient, when he can walk, drags himself about in a dreamy sort of way, or he staggers like a drunken man. There may be nausea and vomiting. In some instances there is diarrhœa.

Stage of fever. The stage of invasion may last for a day or two without a serious rise of temperature occurring. Generally, however, it is of much shorter duration; or it may be altogether wanting, the disease developing abruptly without definite rigor or other warning, the thermometer rising somewhat rapidly to 103° or 104°, or even to 107°, with a corresponding acceleration of pulse and respiration. The rise of temperature is more gradual than is usual in malarial fevers. The skin is now dry and burning, the face bloated, the eyes still more injected, sunken and fixed, the hearing dulled. The tongue is swollen and covered with a creamy fur which rapidly dries and becomes brown or almost black; sordes form on the teeth and about the lips and nostrils. Thirst is intense, prostration extreme, the patient from utter weakness being

hardly able to make himself heard. Sometimes the patient becomes delirious; more generally he sinks into a state of typhoid stupor and prostration, perhaps picking the bedclothes or trying to catch imaginary objects. The delirium is sometimes wildly furious, sometimes fatuous, sometimes of a low muttering type. Coma, convulsions—sometimes of a tetanic character—retention of urine, subsultus tendinum, and other nervous phenomena may occur. Vomiting is in certain cases very frequent; some are constipated, others have diarrhœa. The spleen and liver are usually both enlarged. Urine is scanty, but rarely contains more than a trace of albumin. The pulse, at first full and bounding, in the majority of cases rapidly loses tone, becoming small, frequent, fluttering, dicrotic, intermittent. In the later stages the heart may be dilated, the first sound being feeble or absent. In many, as death approaches, there may be a certain amount of cyanosis.

Stage of adenitis.—In from about two-thirds to nine-tenths of the cases, some time between the first few hours and the fifth day, generally within twenty-four hours, the characteristic bubo or buboes develop. Usually (in 70 per cent.) the bubo forms in the groin, most frequently on the right side, affecting one or more of the femoral glands; less frequently (20 per cent.) it is the axillary glands, and still more rarely (10 per cent.), and most commonly in children, it is the glands at the angle of the lower jaw that are affected. The buboes are usually single; in about one-eighth of the cases, however, they form simultaneously on both sides of the body. Very rarely are buboes formed in the popliteal or in the epitrochlear elbow glands, or in those at the root of the neck. Occasionally buboes occur simultaneously in different parts of the body.

The buboes vary considerably in size. In some instances they are no larger than a walnut; in others they attain the size of a goose's egg. Pain is often very severe; on the other hand, it is sometimes hardly complained of. Besides the enlargement of the gland

itself, there is in most instances distinct infiltration of the surrounding connective tissue.

In a very small proportion of cases what are usually described as carbuncles, but which are in reality small patches of moist gangrenous skin which may gradually involve a large area (Lowson), develop on different parts of the integument. These occur either in the early stage or late in the disease. Sometimes they slough and lead to extensive gangrene.

In favourable cases, sooner or later, after or without the appearance of the bubo, the constitutional symptoms abate with the setting in of a profuse perspiration. The tongue now begins to moisten, the pulse-rate and thermometer to fall, and the mild delirium, if it has been present, to abate. The bubo, however, continues to enlarge and to soften. After a few days, if not opened by the surgeon, it bursts and discharges pus and sloughs, sometimes very evil-smelling. In rare instances suppuration is delayed for weeks; and in some the bubo subsides after a few weeks, or perhaps months, without having broken down. Convalescence, when it occurs, sets in some time between the sixth and tenth day, although it may be delayed for a fortnight or three weeks. Occasionally a pyæmic condition with boils, abscesses, cellulitis, parotitis, or secondary adenitis succeeds the primary fever. The sores left by the buboes and abscesses of plague are extremely indolent and may take a long time—months—to heal.

Hæmorrhages of different kinds are not an unusual feature in plague. Ecchymotic effusions of a purplish or dull red tint, and varying in size from a hemp seed to spots half an inch in diameter, are very often found scattered in greater or less profusion over the skin, especially, according to Lowson, on exposed parts of the body and at the sites of insect bites or of wounds. Larger patches of cutaneous hæmorrhagic effusion do occur, but they are rare. There may be bleeding from the nose, mouth, lungs, stomach, bowel, or kidneys. Hæmorrhages occur with marked

frequency in certain epidemics; they are regarded as evidence of great malignity. Especially malignant are those epidemics in which hæmoptysis, or pneumonia, is a common occurrence.

Abortion almost invariably occurs in pregnant women; the fœtus sometimes shows signs of the disease.

Death may take place at any time in the course of plague. Usually it occurs between the third and fifth days, with symptoms of profound adynamia, heart failure, or perhaps from convulsions, from coma, from internal hæmorrhage, or later, from exhaustion from prolonged fever or suppuration, or from secondary hæmorrhages.

On the other hand, in a certain proportion of cases convalescence sets in and proceeds more or less rapidly. Generally it is a tedious affair, being prolonged by suppuration, sloughing, and similar complications.

Pestis siderans.—In that type of plague which has acquired the name of *pestis siderans* the disease proves rapidly fatal, death occurring some twelve to twenty-four hours from the onset of the symptoms, and before there is time for the development of the bubo. Lowson believes that these cases are pneumonic principally.

Abortive or larval plague (pestis ambulans).—Certain epidemics are distinguished by the larger proportion of mild cases. In such, buboes form and suppurate or resolve, the associated constitutional symptoms being comparatively mild or, perhaps, altogether wanting. In every epidemic there may be cases in which the patient is able to be about, having little, if any, fever, and apparently being little inconvenienced by the disease. Such cases, however, may collapse suddenly.

The occurrence of epidemics of bubo with little or no constitutional symptoms, which precede and follow true plague, have already been alluded to (p. 150) These cases are of great importance in

their bearing on the spread and prevention of the graver disease.

Relapses, though rare, do occur and are dangerous.

Mortality.—The mortality in plague varies in different epidemics. It is usually greatest at the beginning and height of the epidemic. Disregarding those mild epidemics just alluded to, the death-rate may be anything from 60 to 95 per cent. of those attacked. A good deal appears to depend on the social condition of the patient, the attention and nursing he can command, and on the amount of the initial dose of virus. Thus in the late Hong Kong epidemic, whilst the deaths among the indifferently fed, overcrowded, unwashed, and almost unnursed Chinese amounted to 93·4 per cent., it was only 77 per cent. among the Indians, 60 per cent. among the Japanese, and only 18·2 per cent. among the Europeans, a gradation of mortality in general correspondence with the social and hygienic conditions of these different nationalities.

Pathological anatomy and pathology.—After death from plague the surface of the body presents very frequently numerous ecchymotic spots or patches. The number and extent of these vary, apparently, in different epidemics. Sometimes as in the recent Hong Kong epidemic (Lowson) they are few and trifling, having their origin, as mentioned, principally in insect bites. In other epidemics, according to their historians, the cutaneous hæmorrhages have been both extensive and numerous; hence the name Black Death formerly applied to this disease. The characteristic buboes are generally apparent, occasionally there are also furuncles, pustules, and abscesses. Rigor mortis is usually moderate; sometimes *post mortem* muscular contractions, like those of cholera, take place. *Post-mortem* rise of temperature is often observed. Decomposition is said to set in early.

The brain, spinal cord, and their meninges are markedly congested, and there may be an increase

of subarachnoid and ventricular fluid. There are numerous and pronounced *puncta cruenta* on the brain sections, occasionally there may be considerable extravasations of blood into the substance of the brain (mesocephalon and medulla oblongata).

Ecchymoses are common in the pleura as in all serous surfaces; and the contents of the pleura, as those of the other serous cavities, may be sanguineous. Extensive hæmorrhages are occasionally found in the peritoneum, mediastinum, trachea, bowel, pelvis of kidney, ureter, bladder, or in the pleural cavities. The lung frequently shows evidences of bronchitis and hypostatic pneumonia, sometimes hæmorrhagic infarcts and abscesses are found. The right side of the heart and great veins are usually distended with feebly coagulated or fluid blood.

The liver is congested and swollen, and its cells are degenerated. The spleen is enlarged to two or three times its normal size. The mucosa of the alimentary canal as a whole is congested, showing here and there punctate ecchymotic effusions and, occasionally, hæmorrhagic erosions, and even—especially about the ileo-cæcal valve—ulcerations.

Similarly the kidneys are congested, and may exhibit ecchymoses, both on the surface and in the pelvis. The perirenal connective tissue also may be congested and infiltrated. The ureters and the mucous surface of the bladder are often found to be sprinkled with ecchymoses, in which cases the contained urine is generally bloody.

Evidence is invariably discoverable of serious implication of the lymphatic system. One, two or many of the lymphatic glands are inflamed and swollen. Both in and around the glands there is much exudation with hæmorrhagic effusion, hyperplasia of the gland cells, and an enormous multiplication of bacteria. The glands of the groin, of the armpit, and of the neck are particularly affected. On dissection, the superficial buboes are very often found to be connected with extensive, deep-seated adenitis

extending either through the crural ring or down the neck, and involving the pelvic, the abdominal, or the mediastinal glands as the case may be. On cutting into the affected glands, they may be found, according to the period of the disease at which death has occurred, at any stage of inflammation from cellular hyperplasia to suppurative softening. In whatever stage during the activity of the disease death has occurred, there is always evidence of intense hyperæmia in as well as around these glands, a hyperæmia which is specially characterised by a marked tendency to hæmorrhagic effusion. In the earlier stages of the adenitis the specific bacillus is found in the lymph spaces around the follicles: later, it is found in the follicles themselves, in the lymph spaces, and in the medullary cords (Aoyama).

If death have taken place at a very early stage of the disease, the swelling of the lymphatic glands may not be so evident, but it is rare not to find some gland or glands that are characteristically affected. Occasionally, instead of the intense and more or less localised adenitis, a milder but more general enlargement of the lymphatic glands of the entire body is discovered. Sometimes the lymphatic trunks are also markedly implicated in the specific inflammation

Prophylaxis. The prophylaxis of plague, as of other infectious diseases, has to be considered from the standpoint of the community and from that of the individual. As regards the former, it includes measures for preventing the introduction and spread, and for securing the destruction, of the virus.

Quarantine.—All systems of land or sea quarantine directed against plague should take cognisance of the facts that the incubation period of the disease may extend to eight days, and that plague affects certain of the lower animals as well as man. Seven days is the minimum period that should elapse between the time of departure from an infected place, between the date of the last death, and between the arrival of a ship or batch of travellers with cases

of plague in progress among them, and free pratique. Moreover, as Kitasato has shown that the specific bacillus persists in the bodies of those who have recovered from plague for at least three weeks from the cessation of the active disease, convalescents should be isolated for a month before they are allowed to mingle with an uninfected community.

Although Kitasato has stated that the plague bacillus perishes in four days when dried on cover-glasses and protected from sunlight, and in from three to four hours when exposed to sunlight, experience has shown that under certain conditions, as yet unknown, it will survive outside the body for a very much longer period. There is a considerable mass of evidence tending to show that clothes, skins, textile fabrics, and other similar materials, may preserve the virus in an active state for several months. Such articles, therefore, coming from an infected district, more especially if there is any suspicion that they have been soiled by, or have been in proximity to plague patients, should be destroyed or thoroughly disinfected.

In ships coming from an infected port the rats, mice, and suchlike vermin, so far as possible, should be destroyed, thrown overboard and sunk before harbour is entered.

Kitasato found that bouillon cultures of the bacillus were killed in half an hour by a temperature of 80° Cent., and in a few minutes by steam at 100° Cent. Growth of the bacillus did not occur in cultures after exposure for one hour to a 1 per cent. solution of carbolic acid. The bacilli are also killed by a three hours' exposure to milk of lime. These facts serve as a guide to suitable disinfectants; of which the best and most practicable are steam, 1 in 1,000 corrosive sublimate in carbol-sulphuric acid, lysol, chloride of lime in 1 per cent. solution, and carbolic acid in 5 per cent. solution.

In the event of plague breaking out in a community, so soon as the disease is recognised, and provided it be feasible, a double military cordon should

be drawn around the implicated district, and the strictest isolation maintained. The patients should be rigidly isolated in special hospitals, the houses which they had occupied thoroughly disinfected and temporarily evacuated or, better still, especially if unsanitary and of small value, destroyed by fire. The clothes and bedding of all patients should be burned. The dead, with as little delay as possible, should be buried in deep graves, or cremated. Rats and mice should be poisoned or otherwise destroyed, and their bodies burned. Besides such special measures, general sanitation should be scrupulously carried out. The diffusion of plague by railways must be carefully guarded against.

In India the compulsory inspection of all dead bodies prior to burial has been found a valuable measure for discovering infected houses and localities.

In all efforts to control the introduction and spread of plague cases of *pestis ambulans* must be sought out and treated with as much respect as the more virulent forms of the disease.

It is very questionable if in practice any system of rigid quarantine, no matter how carefully devised and theoretically perfect, is ever absolutely protective. Its working is necessarily at the mercy of a large number of individuals, any one of whom, either from incompetence or from dishonesty, may permit its regulations to be broken through. Even if the introduction of plague by man could be prevented in this way, it is difficult to see how its introduction by rats or mice could be effectually guarded against. Quarantine may, and doubtless does, keep out a proportion of the infected, and to this extent it does some good; but it must be combined with careful general sanitation, with thorough disinfection, with the destruction of all discharges and fomites, with the speedy discovery and isolation of the sick, with the evacuation of infected houses and even of neighbourhoods, and with the wholesale destruction of vermin. These latter things English experience has shown to be far more certain than any system of quarantine;

it was only in deference to Continental views that quarantine, in the ancient sense of the word, was practised in Great Britain against plague and another disease—yellow fever. A rational quarantine, plus rational plague measures—isolation of sick, separation of suspects, disinfection—is what is wanted.

Personal prophylaxis.—As regards the individual all unnecessary visits, either to plague patients or to plague neighbourhoods, should be avoided and, if possible, prevented. The attendants on the sick, especially, ought to take care that the ventilation of the sick room is thorough, that cubic space is abundant, and that the utmost cleanliness is practised. Nurses must not hang over patients unnecessarily ; they must also be careful to seal up and cover any wounds, no matter how trifling, they may have on their hands ; they must go into the open air frequently, and not remain in the wards too many hours at a stretch ; they must employ disinfectants freely on themselves and on the excreta of their patients, and use a disinfectant mouth wash from time to time ; they must be careful to wash hands and face before eating ; and they must never partake of food or drink in the ward or sick room. By carefully observing these common-sense precautions the risk in attending plague patients is very much reduced, and is certainly very much less than that attending the nursing of cases of typhus exanthematicus. Those engaged on plague duties should wear boots and have the legs protected by trousers tied round the ankles or, better, by putties. Leather gloves are advisable if there is much handling of furniture or of anything likely to abrade the skin. Hospital work is only dangerous when patients are allowed to lie in their infected clothing, when disinfectants are not properly used, and when attendants are careless, stupid, or rash.*

* Haffkine practised during the Bombay epidemic a system of prophylactic inoculation. A description of his method will be found in the *Brit. Med. Jour.* of June 12, 1897. The reaction produced is severe. The figures, though encouraging, are not conclusive as to the value of the method (*Brit. Med. Jour.*, Dec. 25, 1897).

Treatment. Hitherto the treatment of plague has been mainly symptomatic. In attempting to relieve symptoms the asthenic tendencies of the disease must ever be borne in mind, and depressant remedies of all kinds carefully avoided.

During the earlier stages, when headache and perhaps high fever are urgent, much relief may be obtained from ice bags to the head and neck. If it be deemed advisable to attempt to lower temperature, sponging of the body every hour with warm water is a much safer measure than the employment of such antipyretics as antipyrin and similar drugs. Vomiting, according to Lowson, is usually relieved by a full dose of calomel followed by a saline. If this does not succeed, or if diarrhœa be present, he recommends ice pills and an effervescing mixture containing morphia and hydrocyanic acid. Sinapisms to the epigastrium are also useful. Later, when the pulse begins to fail, the same authority recommends strychnia, with or without carbonate of ammonia, in preference to digitalis or strophanthus. Strychnia, he says, should be used as a routine treatment, and commenced early in the disease. In collapse, stimulants of various kinds, including strong ammonia to the nostrils and ether hypodermically, are indicated; they sometimes succeed in resuscitating a sinking patient. Given with judgment, Lowson found that morphia was by far the best hypnotic. At the commencement one-eighth to half a grain hypodermically relieves suffering and procures sleep; later, one-eighth of a grain suffices. Hyoscine (one two-hundredth to one seventy fifth grain), or chloral (twenty grains) and bromide of potassium (thirty grains) are of service for the same purpose. Diarrhœa, if urgent, is best treated by intestinal antiseptics, as salol in 10-grain doses every four hours. The buboes in the early stage may be treated with applications of glycerine and belladonna. Should they become red and inflamed they must be poulticed and, on softening occurring, incised and dressed with iodoform. Indolent

bubonic swellings should be treated with iodine liniment. Feeding and stimulation are to be conducted on ordinary principles.

Serum therapy.—Yersin, Calmette, and Borrel (*Ann. de l'Inst. Pasteur*, vol. ix., 1895, p. 589) have shown that intravenous, intraperitoneal, and subcutaneous injections of gelatine cultures of plague bacillus mixed with a little bouillon and heated for one hour to 58° Cent., if employed in doses just short of producing a fatal issue, and repeated three or four times at intervals of fifteen days, render rabbits immune to the plague bacillus. The heating kills the bacillus, but does not destroy its toxins, which, at first, give rise to a very smart but, with each repetition of the injection, diminishing reaction. They further found that the serum of an immunised animal, if injected into an unprotected rabbit, exercised both an immunising and a therapeutic influence. An unprotected rabbit was inoculated with a virulent culture of the bacillus, and twelve hours afterwards with the serum. The progress of the disease, which would otherwise have certainly proved fatal, was at once arrested and the animal recovered. They then immunised a horse by intravenous injections of living virulent cultures. After several injections made at intervals (the second after twenty days), they found that reaction, from being intense, became shorter and less, and that the serum of the animal was now both preventive and curative of inoculated plague in rabbits, guinea-pigs, and mice.

Accounts had led us to infer that the value of this discovery had been practically established for man. Of twenty-six cases of plague in China treated with Yersin's antipest serum, twenty-four are reported to have recovered. Further experience in India has not confirmed these brilliant results, the serum treatment of plague there having, so far, proved a failure.

CHAPTER IX.

DENGUE.

Definition.—Dengue—a word derived, according to Hirsch, from the Spanish equivalent of the English word "dandy"—is the name applied to a specific and highly infectious fever peculiar to warm climates. It occurs usually in widespread epidemics. Once introduced into a community, it extends with great rapidity, affecting a large proportion of the inhabitants, much in the same way as the more familiar influenza, with which dengue has by some been confounded. It differs, however, from influenza in many respects, chiefly in being attended with a well-marked rubeoloid eruption and peculiarly severe rheumatic-like pains in the joints and limbs, and in not being accompanied or followed by pulmonary and other serious complications.

Geographical distribution and mode of spread.—Most parts of the tropical world have been visited at some time or another by dengue. From a study of the dates of the various epidemics, it would seem that there is a tendency for it to assume pandemic characters about once in every twenty years. The last great wave occurred in the early 'seventies. Perhaps of all places in the world it is most frequently met with in the West Indies.

Recently dengue has appeared in Syria, Asia Minor, and on the Ægean shores of Greece and Turkey, extending as far north as the southern shore of the Black Sea. Earlier in the century, in America, it was seen as far north as Charleston and Philadelphia in the United States, and as far south as San Paulo in the Brazils.

Like other infectious diseases, dengue tends to advance along the trade routes and lines of communication. Thus, starting from Zanzibar, the epidemic of 1870–73 first reached Aden. From this port it travelled to Suez on the one side, and to India on the other. Passing to Singapore, it followed the trade routes to Cochin China and China, spreading at the same time to the islands of the Eastern Archipelago. From India it was carried by coolies to Mauritius and Réunion in 1873.

An epidemic which I witnessed in Amoy illustrated very well a characteristic feature of dengue epidemics—namely, the peculiar suddenness of their rise and extension, and the general prevalence of the disease in an affected community. I am under the mark when I say that in the particular epidemic referred to quite 75 per cent. of natives and foreigners were attacked within a very few weeks. All ages were alike subject to it; so were all occupations, both sexes, and every condition of life. About the first week in August I heard that a peculiar disease had appeared in the town; by the end of the second week the cases were numerous, whole families being prostrated at a time. A week later the cases were still more numerous, and by the end of the month so general was the disease that the business of the town was seriously interfered with. By the end of the following month—that is to say, in about eight weeks from the first appearance of the epidemic—all the susceptible apparently had passed through it, and, so far as Amoy residents were concerned, the disease was at an end, cases only occurring for a few weeks longer in visitors from unaffected districts. This course seems to be fairly typical of all dengue epidemics.

Ætiology.—*Germ.*—Nothing is known as to the virus of this disease. Doubtless it is similar in its nature to that of all the other exanthematous fevers, diseases to which dengue is manifestly intimately allied.

Influence of meteorological conditions. — When dengue spreads beyond its ordinary geographical limits, as, for example, in the epidemics of Philadelphia and Asia Minor, the extension occurs only during the hottest part of the year in the late summer and early autumn Hitherto, such epidemics have been arrested on the approach of winter. Even when occurring within what may be designated as its normal geographical limit, dengue prevails principally, though not exclusively, during the hottest part of the year. High temperature seems, therefore, to be one of the conditions it demands.

Epidemics occur indifferently during the dry or the rainy season, the hygrometric condition of the atmosphere being without manifest influence.

Usually a coast disease. It would appear that dengue, like yellow fever, prefers the coast line, and the deltas and valleys of great rivers, to the interior of continents. There are exceptions to this rule, however, for in 1870–73 it spread all over India. The distribution and concentration of population on the sea-board and along rivers, and the freedom of communication between communities so placed, may have some influence in determining this clinging to such localities.

As a rule, elevated places enjoy what is at all events a relative immunity ; if the disease is introduced into such localities, it does not spread. To this, again, there are exceptions, for the Syrian epidemic referred to prevailed in certain spots 4,000 to 5,000 feet above the sea.

Symptoms. *Initial fever and eruption.*—An attack of dengue may be preceded for a few hours by a feeling of malaise or, perhaps, by painful rheumatic-like twinges in a limb, toe, finger, or joint. Usually it sets in quite suddenly. A patient, describing his experience, said that in the morning he got up, as usual, feeling quite well, but before he could complete his dressing he was so prostrated by pain and fever that further exertion was impossible, and he had to

crawl back to bed again. Similar stories, illustrative of the suddenness of incidence of the symptoms, circulate during every epidemic of dengue. Sometimes the fever is ushered in by a feeling of chilliness or even by a smart rigor; sometimes a deep flushing of the face is the first sign of the disease.

However introduced, fever rapidly increases. The head and eyeballs quickly begin to ache excessively, and some limb or joint, or even the whole body, is racked with the peculiar stiff, rheumatic-like pains which, as the patient soon discovers, are very much aggravated by movement. The loins are the seat of great discomfort, amounting in some cases to actual pain, the face—particularly the lower part of the forehead, round the eyes, and over the malar bones—becomes suffused a deep purple, and often the skin over part or the whole of the body and all visible mucous surfaces are more or less flushed, that of the mouth and throat being sore from congestion and perhaps from small superficial ulcers. The eyes are usually much injected; very often the whole face is bloated and swollen. This congested erythematous state of the skin constitutes the so-called initial eruption.

These symptoms becoming in severe cases rapidly intensified, the patient, in a few hours, is completely prostrated. His pulse has risen to 120 or more; his temperature to 103°, in some cases to 105°, or even to 106°. He is unable to move owing to the intense headache, the severe pain in limbs and loins, and the profound sense of febrile prostration. The skin, for the most part hot and dry, may be moistened from time to time by an abortive perspiration. Gastric oppression is apt to be urgent, and vomiting may occur. Gradually the tongue acquires a moist, creamy fur which, as the fever progresses, tends to become dry and yellow.

Defervescence.—In this condition the patient may continue from one to three or four days, the fever declining somewhat after the first day. In the vast majority of cases this, the first and most acute

stage, is abruptly terminated about the end of the second day by crisis of diaphoresis, diarrhœa, diuresis, or epistaxis. When epistaxis occurs the relief to the headache is great and immediate. On the occurrence of crisis the erythematous condition of the skin, if it has not already disappeared, now rapidly subsides. In a proportion of cases crisis does not occur, the fever slowly declining during a period of three or four days. Thus the urgent symptoms abate, and the patient rapidly, or more slowly, passes from what, in many cases, may be described as the agony of the first stage to the comparative calm and comfort of the second.

The interval. — When the second stage is thoroughly established and the thermometer has sunk to normal, the patient is sufficiently well to leave his bed and even to attend to business. An occasional twinge in the leg, arm, or finger, or a tenderness of the soles of the feet, and perhaps giddiness in walking, may remind him of what he has gone through and warn him that he is not quite well yet. But the tongue cleans, the appetite returns to some extent, and he feels moderately comfortable.

Terminal fever and eruption. — This state of matters continues to the fourth, fifth, sixth, or even to the seventh day, counting from the commencement of the illness. Then there is generally a return of fever, slight in most cases, more severe in others; it is usually of very short duration—a few hours, perhaps. Sometimes this secondary fever does not occur; very often it is overlooked. With the return of the fever an eruption of a roseolar character appears. The pains likewise return, perhaps in more than their original severity. The fever subsides in a few hours; but the eruption, though at times very evanescent, may keep out for two or three days longer, to be followed very generally by an imperfect furfuraceous desquamation. It seldom happens that the fever or pains of this stage keep the patient in

bed, although that is the best place for him if a comfortable and speedy convalescence is desired. Rarely, in this secondary fever, does the thermometer rise to 103°. The temperature falls rapidly to below the normal line on the setting in of diaphoresis, or diarrhœa, or of some other form of crisis.

Characters of the eruption.—The terminal eruption of dengue possesses very definite characters. It is absent in a very few cases only; it is quite possible, in many of those cases in which it is supposed to be absent, that, being slight, it is overlooked. As stated, the eruption is roseolar in character. It usually commences on the palms and backs of the hands, extending for a short distance up the forearms. Its development is often associated with sensations of pricking and tingling. On the palms of the hands the spots are at first about the size of a small pea, circular, dusky red, and sometimes slightly elevated. The eruption quickly extends, and is best seen on the back, the chest, the upper arms, and the thighs. In these situations it appears at first as isolated, slightly elevated, circular, reddish brown, rubeoloid spots, from one-eighth to one-half of an inch in diameter, thickly scattered over the surface, each spot being isolated and surrounded by sound skin. After a time the spots, enlarging, may coalesce in places; thus irregular red patches from one to three inches in diameter are formed. Or, perhaps, there is a general coalescence of spots, isolating here and there patches of sound skin; in the latter case the islands of sound skin give rise, at first sight, to the impression that they constitute the eruption—a pale eruption, as it were, on a scarlet ground. In a few instances the whole integument may be covered with one unbroken sheet of red. The rash is usually most profuse on the hands, wrists, elbows, and knees, and in these situations it is generally coalescent, and there, too, it may be detected though absent elsewhere. The spots disappear on pressure, and never become

petechial, or only very rarely. They fade in the order in which they appear—first on the wrist and hands, then on the neck, face, thighs and body, and, last of all, on the legs and feet.

Desquamation.—Desquamation may go on for two or three weeks. In many it is trifling in amount; for the most part it is furfuraceous. Rarely does the epidermis peel off in flakes of any magnitude; never in the broad sheets seen after scarlatina. Often for a day or two desquamation is accompanied by intense pruritus.

Convalescence.—In some instances the disease may be said to finish its course with the fading of the terminal eruption; appetite and strength gradually return, and the patient, after a few days of debility, feels quite well again and able to work.

The rheumatoid pains.—But with many, indeed with most, their troubles do not end so soon. For days or weeks some muscle, tendon, or joint is the seat of the peculiar pains which may become so severe as to send their victim back to bed again. Sometimes, three or four weeks after all apparent trace of the disease has vanished, a joint or a muscle will be suddenly disabled by an attack of this description. This may occur in patients who, during the acute stage, suffered perhaps but little or no pain. A finger or toe, or a joint of a finger or of a toe, may alone suffer. Of all the joints perhaps the knee is most frequently affected; but wrists or shoulders are often attacked, and their associated muscles may even undergo considerable atrophy from enforced disuse. The soles of the feet, too, and the tarsal articulations are favourite sites.

The pains of dengue, both those occurring during the initial fever as well as those that may be regarded as sequelæ, are difficult to locate with precision, the joints or muscles affected may be percussed, pressed, or moved with impunity. Du Brun locates those associated with the knee in the thigh muscles, which, he says, are painful on deep pressure.

The pains are worst usually on getting out of bed in the morning, and on moving the affected part after it has been at rest for some time. They are relieved somewhat by rest and warmth. Passive movements are, as I have said, not painful, but any resistance to the movement of the limb may cause acute suffering. When a muscle is affected the pain is accompanied by a sense of powerlessness.

Other complications and sequelæ.—Convalescence may be very much delayed by the persistence of these pains; also by anorexia, by general debility, sleeplessness, evanescent feverish attacks, boils, urticarial, lichenoid, and papular eruptions, and by troublesome pruritus. Among sequelæ and complications may be mentioned enlargement of the lymphatic glands—particularly the superficial cervical—orchitis, possibly endocarditis and pericarditis, hyperpyrexia, and hæmorrhages from the mouth, nose, bowel, and uterus. Miscarriage is rare. The urine sometimes contains a trace of albumin, but true nephritis does not occur.

Such, briefly, is a description of the dengue observed by myself in Amoy in 1872. It would appear, however, judging from the published descriptions, that there is considerable variety in the symptoms of this disease in different places and in different epidemics. Some authors mention swelling of one or more joints as a common and prominent symptom; others refer to metastasis of the pains, enlargement of the submaxillary glands, orchitis, and so forth, as being frequently present. These, in my experience, were excessively rare. However this may be, the essential symptoms in well-marked cases are the same practically everywhere, and in all epidemics. Nearly all writers accentuate as the leading and characteristic symptoms the suddenness of the rise of the temperature, the initial stage of skin congestion, the pains, and the terminal eruption.

Relapses are not uncommon in dengue, and second and even third attacks during the same epidemic

have been recorded. As a rule, however, susceptibility to the disease is exhausted by one attack.

The *incubation period* seems to be somewhat variable. It is certainly not a long one. I have seen a case in which it could not have exceeded twenty-four hours. Some observers place it at five and even seven days; this, I feel sure, is an overestimate. One to three days seems to be near the truth.

Diagnosis.—Dengue must not be confounded with rötheln, scarlatina, measles, syphilitic roseola, influenza, rheumatic and malarial fevers. A knowledge of the distinctive features of these diseases, and the fact that dengue is attended with a rash and with articular pains, and that it occurs in great and rapidly-spreading epidemics, should prevent any serious error in diagnosis.

Mortality.—In uncomplicated dengue the mortality may be said to be almost *nil.* In the case of very young children, convulsions and delirium may occur and cause some anxiety; and in the aged and infirm, and in those suffering from chronic exhausting disease, an attack of dengue may prove a serious complication. Charles describes a pernicious form which, though rare, was very much dreaded in Calcutta. In these cases the lungs became œdematous, and the patient, growing drowsy and cyanotic, rapidly passed into a comatose condition, with a tendency to hyperpyrexia, and died. Some writers state that the gravity of any given case is in direct proportion to the abundance of the eruption; others deny this. In Europeans an attack of dengue very often leads to a condition of debility necessitating temporary change of climate, or even return to Europe. In both Europeans and natives the attendant lowering of the resistive powers predisposes to other and more dangerous diseases, such as malaria, yellow fever, dysentery, phthisis, and so forth; consequently dengue, otherwise a benign disease, may become a source of public danger. It is probable that it is in this indirect

way that the general mortality rises during a visitation of this disease, as has been observed in several epidemics.

Treatment.—Were it possible to secure perfect isolation for the individual during an epidemic of dengue, doubtless he would escape the disease. Even comparative isolation is attended with diminished liability. In Amoy, in the epidemic of 1872, those foreigners who lived in a more or less isolated suburban situation were very much less affected than were those who lived in the native town, or than those whose occupations threw them much into contact with the natives. But though this and similar facts point to the theoretical possibility of avoiding dengue during an epidemic, in the ordinary conditions of life in the tropics prophylactic measures, such as they would suggest, are impracticable.

Like the allied fevers, dengue runs a definite course; therefore it is useless to attempt to cut it short. The patient should go to bed so soon as he feels ill, and he should keep his room till the terminal eruption has quite disappeared and he feels well again. Ten days is not too long to allow in severe attacks. As in influenza, light liquid diet, rest, and the avoidance of chill conduce powerfully to a speedy and sound convalescence. At the outset of the fever some saline diaphoretic mixture, with aconite, may be prescribed with advantage. If the pains be severe and the fever high, antipyrin, or phenacetin, or belladonna will give great relief. Cold applications to the head are comforting. If the temperature rises to 105° or over, cold sponging or the cold bath ought to be had recourse to. If the pains continue very distressing, a hypodermic injection of morphia will afford welcome relief and do no harm. Purgatives and emetics should be avoided unless pronounced constipation, or a history of surfeit, urgently demands their exhibition. The pain caused by the muscular movements entailed by the efficient action of purgatives more than counterbalances any

advantage the latter might otherwise bring. Wine in the early stage is not advisable. Freshly made lemonade or iced water will be found the most acceptable drink during the fever.

For the pains experienced during convalescence, rubbing with opium or belladonna liniment, gentle massage, electricity, salicylates, small doses of iodide of potassium and quinine have been advocated. Debility and anorexia indicate tonics such as quinine, strychnine, mineral acids, vegetable bitters, and change of air.

CHAPTER X.

MALTA OR MEDITERRANEAN FEVER.

(*Febris undulans*, Hughes).

Definition.—Malta fever—a disease probably of pythogenic origin, of low mortality, and of limited geographical range—is characterised in its more typical form by, or, rather, is made up of, a series of febrile attacks; each individual attack, after lasting one or more weeks, gradually subsiding into a period of absolute or relative apyrexia of several days' or several weeks' duration. Each spell of relative apyrexia is followed by a period of fever, which is again succeeded by relative apyrexia. So the disease continues more or less indefinitely for weeks or months. Common and characteristic complications are rheumatic-like swelling of joints, profuse diaphoresis, anæmia, liability to orchitis and neuralgic affections.

The duration of the illness is uncertain; it may be anything from three or four weeks to as many months, often longer and even up to eighteen months.

Geographical distribution.—Malta or Mediterranean fever is somewhat unfortunately named, for it is by no means certain that the disease so designated is confined to Malta, or to the Mediterranean even. It is very common there, particularly in Malta; but this is all that can be said with confidence about its geographical range. It is highly probable, however, that the same, or a similar, fever occurs in many parts of the tropical world, having been confounded hitherto with malarial fever.*

* On the strength of some experiments, analogous to those of Widal's typhoid culture agglutination and sediment test, Wright has lately asserted that Malta fever occurs in India. On clinical grounds this has been denied by others.

This disease is specially interesting to English military surgeons, as it is extremely prevalent at times in the garrisons of Gibraltar and Malta; although only occasionally proving fatal, it is a fruitful source of inefficiency and invaliding there.

History.—Formerly it was confounded with typhoid and malarial fever; by some it is still regarded as but a phase of one or other of these. The labours of clinical observers, from Marston (1861) to Maclean (1885), and more especially the recent bacteriological researches of Bruce, Hughes, and Gipps, have established it as a special disease; in the future it must be regarded as such. It requires to be renamed, however, and until this is done there will continue to be confusion on the subject.

Symptoms.—Malta fever begins generally with lassitude and malaise, such as we associate with the incubation of many specific fevers, particularly with typhoid. There is headache, boneache, anorexia, and so forth. At first the patient may go about his work as usual; gradually the daily task becomes too much for him, and he has to take to bed. Headache may now become intense, and, in addition, the patient will suffer from thirst and constipation. At the commencement the symptoms, with the exception that there is very rarely diarrhœa, resemble those of typhoid. There are no rose spots, however, then or at any subsequent period. There is evidence in the coated tongue, the congested pharynx, the anorexia, and the epigastric tenderness, of gastric catarrh; and the occasional cough and the harsh, unsatisfactory breathing at the bases of the lungs indicate some degree of pulmonary congestion. There may also be delirium at night. The fever is usually of a remittent type, the thermometer rising towards evening and falling during the night, the patient becoming bathed in a profuse perspiration towards morning. The spleen and the liver, but especially the former, are somewhat enlarged and, perhaps, tender. Lumbar pain may be urgent.

After a week or two of this type of fever, specially distinguished by pains and perspirations, the tongue begins to clean, and the appetite may revive; but, notwithstanding these signs of amendment, the patient still remains listless, and liable to headache and constipation. He continues feverish, and at times perspires profusely. Gradually however, although anæmic and excessively weak, subjective symptoms become less urgent; he sleeps well now, he has no delirium at night, and he can take his food, and this even although the body temperature may still range too high.

About this time the peculiar fleeting rheumatic-like affections of the joints, so characteristic of the disease, show themselves in a large proportion of cases. One day a knee is hot, swollen, and tender; next day this joint may be well, but another joint is affected; and so this metastatic rheumatic-like condition may go on until nearly all the joints of the body have been involved one after the other. The patient may suffer also from neuralgia in different nerves—intercostal, sciatic, and so on. Orchitis is an occasional complication. In some cases these complications are severe and characteristic; in others they may be mild, or absent altogether. In this respect the same infinite variety shows itself, as regards complications, as in other specific fevers.

Perhaps the most characteristic feature of Malta fever is the peculiar behaviour of the temperature. In a mild case there may be a gradual ladder-like rise through a week or ten days to 103° or 104°, and then, through another week or so, a gradual ladder-like fall to normal, the fever, which is of a continued or slightly remitting type, leaving for good without complication of any sort in about three weeks.

Such mild cases are the exception. Usually, after a few days of apyrexia, absolute or relative, the fever wakes up again and runs a similar course, the relapse being in its turn followed by an interval of apyrexia, which is again followed by another relapse; and so on during several months.

Generally remittent or nearly continued in type, occasionally, in some instances, the fever exhibits distinct daily intermissions, the temperature chart suggesting some septic invasion or an ordinary intermittent malarial fever. But there is no evidence of suppuration to be found anywhere; neither, if we examine the blood, is the plasmodium malariæ to be discovered; nor is the quotidian rise of temperature accompanied by any ague-like rigor, or at most, only by a feeling of chilliness; nor is the disease amenable in any way to quinine.

Sequelæ, mortality, and types.—As a rule, the most serious consequences of Malta fever are the debility it entails, the profound anæmia, the rheumatic-like pains, and the neuralgiæ. There is little risk to life; the mortality does not exceed 2 per cent. When death occurs, it is usually from suddenly developed hyperpyrexia; occasionally it is brought about by exhaustion, or by some pulmonary complication such as pneumonia. In a few instances the fever is of a fulminating type, rapidly ending in death from hyperpyrexia. Hughes, who has made an elaborate study of this disease, designates such cases "malignant." Those cases with well-marked waves of fever he calls "undulating"; those with ague-like diurnal fluctuations of temperature, "intermittent." The combination of types is infinite, an "undulating" case sometimes assuming "intermittent" characters, or *vice versâ;* malignant hyperpyrexial symptoms may supervene in either type and at any period in their progress.

Diagnosis.—The diagnosis of Malta fever from typhoid is, of course, a highly important practical matter. It is exceedingly difficult in the early stages. Principal reliance has to be placed on the absence of rose spots, the absence of diarrhœa, the presence of joint complications, the sweats, and, if available, the culture precipitation test. Wright has shown that the germ of Malta fever reacts to the serum test in the same way as the bacillus typhosus. After the

fever has gone on for several weeks diagnosis is, of course, easy; in the early stages, on clinical grounds alone it may be almost impossible. It may be that it is only on the *post-mortem* table that we have the assurance, from the absence of ulceration in the ileum, that we have had to deal with a case of Malta fever. Tuberculosis, abscess, empyema, and all other causes of continued high temperature, have to be carefully excluded in attempting a diagnosis.

Pathological anatomy and pathology.—This disease has almost no pathological anatomy. The spleen is the only viscus of which it can be said that it is distinctly diseased. In Malta fever this organ is distinctly enlarged, soft, and diffluent; on microscopical examination, the lymphoid cells are found to be increased in number.

Ætiology.—*The micrococcus melitensis.*—Most important fact of all in connection with the spleen is the presence in it of a peculiar bacterium—the micrococcus melitensis, as it has been called. For this discovery, made in 1887, we are indebted to Surgeon-Major David Bruce of the Army Medical Staff. Unfortunately, the bacterium does not occur in the general circulation, and therefore Bruce's discovery is of little direct use in diagnosis; but pathologically it is of great importance, as it enables us to say positively that this so-called Malta fever is a distinct disease, altogether different from either typhoid or malaria. The organism is present in the pulp of the spleen, from which it can be separated by cultivation. Bruce found it in this way in ten fatal cases. His results have been confirmed by Hughes and Gipps, the former of whom found the same bacterium in fifteen cases, the latter in two. Injections of pure cultures gave rise to a similar disease in monkeys, from whose blood the micrococcus was recovered, cultivated afresh, and, on injection into other monkeys, again gave rise to the disease.

The micrococcus melitensis is somewhat oval in shape, and measures ·33 micromillimetre in

diameter. It occurs generally singly, often in pairs, sometimes in fours, but never in longer chains. It is readily stained by a watery solution of gentian violet, and is best cultivated in a 1½ per cent. very feebly alkaline, peptonised agar-agar beef jelly, in which, soon after inoculation, it appears as minute, clear, pearly spots. After thirty-six hours the cultures become a transparent amber; later they are opaque. No liquefaction occurs.

Influence of age and residence.—The most susceptible age as regards Malta fever is between the sixth and the thirtieth year. Very young children and old people are less frequently attacked. Length of residence does not influence susceptibility.

Influence of season.—In Malta and other places where the disease is endemic this fever occasionally assumes an epidemic character. The period of its greatest prevalence is the season of lowest rainfall, embracing June, July, and August; differing in this latter respect from typhoid, which, in that island, is more prevalent during the three succeeding months—September, October, and November.

Local causes.—Great difference of opinion obtains both as regards the causes giving rise to this fever, and also as to those influencing its prevalence. The water supply is blamed by some; others attribute the disease to fæcal saturation of the soil, and so on. The disease tends to occur in particular houses, barracks, and rooms, manifestly originating in limited foci of infection. The weight of evidence points to a fæcal origin of the virus; and, also, to its diffusion by air currents, and not by food or water. There is no certainty on these points, nor will there be until the habits and haunts of micrococcus melitensis outside the human body are definitely ascertained.

Influence of social conditions.—All classes are liable to this disease; the officer and his family as well as the soldier in barracks.

Not infectious.—So far as known, Malta fever is

not transmitted directly from one person to another; that is to say, it is not directly communicable from the sick to the healthy.

Incubation period.—The period of incubation is difficult to fix. Cases have occurred as early as six days after arrival in Malta; on the other hand, the disease has shown itself as late as fourteen and seventeen days after the subject of it has quitted Malta, and perhaps after arrival in England.

Immunity. — Bruce considers that one attack confers immunity from subsequent attacks; other authorities hold a different opinion, believing that one attack, so far from conferring immunity, actually predisposes to subsequent attacks.

Treatment.—Malta and those Mediterranean ports in which this fever is endemic should be avoided by pleasure- and health-seekers during the summer months. Those who are obliged to live there all the year round would do well at this season to leave the towns and reside in the country. As a matter of precaution, in the endemic area the drinking water, food, and drains, ought at all seasons to have especial care bestowed on them.

When the diagnosis is sure, it is well to give a purge—none better than calomel and jalap—and to instruct the attendants to keep the patient's temperature systematically below 103° by cold sponging with vinegar and water or, if necessary, by cold bath or ice variously applied. In view of the prolonged nature of the fever, this measure is one of importance; at the same time, such treatment need not be applied too energetically, or so as to depress; a fall of 2° or 3° is all that is desirable.

Quinine and, on account of the joint affection, the salicylates are very generally prescribed. Both are useless, if not injurious. Antipyrin and other antipyretics are also often given to bring down temperature; but the wisdom of employing depressing drugs in so chronic and asthenic a disease as Malta fever is, to say the least, questionable. Any threat of

hyperpyrexia is best met as directed, namely, by early employment of sponging, the wet pack, or, if necessary, by the cold bath. Sleeplessness may demand hypnotics; headache, if severe, moderate doses of antipyrin; inflamed joints or testes, the usual local applications; constipation, enemata or aperients. In fact, the treatment of Malta fever resolves itself into a treatment of symptoms.

The diet at first should consist of milk; later, of broths and eggs and, if necessary, stimulants. Solid food must not be given until all fever has disappeared, and the tongue has remained clear for at least ten days. Lemonade or lime juice should be given after a time; not merely as a pleasant, thirst-relieving beverage, but with a view to averting scurvy—not at all an improbable complication if the diet is too restricted over a long period. The return to solid food must be made with the greatest circumspection; imprudence in this respect may bring on relapse.

Flannel clothing should be worn and frequently changed if there is much sweating.

Change of climate is not so necessary as in malarial affections, seeing, on the one hand, that the disease may persist in England; and, on the other, that it may gradually wear out in Malta. It is not desirable to move a patient when fever runs high, or when debility is very great, or when the cool and healthy season in the Mediterranean is at hand. It must be considered that at this time winter is approaching in England, with climatic conditions very unsuitable for a patient who has become anæmic and debilitated from a long course of fever; at this season he would do much better in Malta or Gibraltar. When, however, the case occurs early in the summer, or runs over the winter, then, in order to avoid the heat of the Mediterranean, change to England, if at all feasible and if it can be comfortably effected, should be advised.

CHAPTER XI.

JAPANESE RIVER FEVER—NASHA FEVER—KALA-AZAR—TROPICAL TYPHOID—TYPHO-MALARIAL FEVER.

THE RIVER FEVER OF JAPAN (SHIMA MUSHI).

Definition.—An acute endemic disease running a definite course. It is characterised by the presence on the skin of an initial eschar, followed by an ulcer, inflammation of the lymphatics, fever, an exanthematous eruption, bronchitis, and conjunctivitis. It is attended by a considerable mortality.

History.—This disease was first described by Palm in 1878, and subsequently, and more fully, by Baelz and Kawakami.

Geographical and seasonal distribution.—So far as known, shima mushi is confined to the banks of two rivers on the west side of the island of Nippon—the Shinanogawa and one of its tributaries, and the Omonogawa. Every spring these rivers inundate large tracts of country. Later in the year hemp is raised on strips of the inundated district. The crop is reaped in July and August, and it is solely among those engaged in harvesting and handling this hemp that the disease occurs. It is not communicable by the sick to the healthy. It is transportable in the hemp to a very limited extent; but it is only in limited spots here and there in the endemic districts that it can originate.

Symptoms.—After an incubation period of from four to seven days the disease usually begins with malaise, frontal and temporal headache, anorexia, chills alternating with flushes of heat, and prostration. Presently the patient becomes conscious of pain and

tenderness in the lymphatic glands either of the groin, or of the armpit, or of the neck. On inspecting the skin of the corresponding lymphatic area there is discovered—usually about the genitals or armpits—a small (2 to 4 mm.), round, dark, tough, firmly adherent eschar, surrounded by a painless, livid red areola of superficial congestion. Occasionally two or three such eschars are discovered. Although a line of tenderness may be traced from the sore to the swollen, hard, and sensitive glands, no well-defined cord of lymphangitis can be made out. The superficial lymphatic glands of the rest of the body, especially those on the opposite side corresponding to the glands primarily affected, are also, but more slightly, enlarged.

Fever of a more or less continued type now sets in, the thermometer mounting in the course of five or six days to 40° or 41° Cent. The conjunctivæ become injected, and the eyes somewhat prominent; at the same time a considerable bronchitis gives rise to harassing cough. The pulse is full and strong, ranging rather low—80 to 100—for the degree of fever present. The spleen is moderately but distinctly enlarged, and there is marked constipation.

About the sixth or seventh day an exanthem of large dark red papules appears on the face, tending to become confluent on the cheeks. The eruption then extends to the forearms, legs, and trunk, but is less pronounced on the upper arms, thighs, neck, and palate. Simultaneously with the papules a minute lichenous eruption breaks out on the forearms and trunk. These eruptions last usually from four to seven days; if but slightly marked, they may fade in twenty-four hours.

The patients during the height of the fever are flushed, and at night, it may be, delirious. They complain incessantly, probably on account of a general hyperæsthesia of skin and muscles. Deafness is also a feature.

As the disease advances the symptoms become

more urgent; the conjunctivitis is intensified, the cough becomes incessant, the tongue dries, the lips crack and bleed, and there may be from time to time profuse perspiration. By the end of the second week —sooner or later according to the severity of the case—the fever begins to remit, the tongue to clean, and, after a few days more, temperature falls to normal, and the patient speedily convalesces. Diarrhœa or diuresis may occur during the decline of the fever. The circular, sharp-edged, deep ulcer left after the separation of the primary eschar—an event which usually takes place during the second week—now begins to heal, and the enlargement of the glands gradually to subside.

Such is the course of a moderately severe case. In some instances, however, the constitutional disturbance is very slight, although the primary eschar may be well marked and perhaps extensive. On the other hand, the fever may be much more violent, and complications such as parotitis, melæna, coma, mania, cardiac failure, or œdema of the lungs may end in death. Similarly the duration of the disease varies, according to severity, from one to four weeks, three weeks being about the average.

Pregnant women contracting shima mushi mostly abort and die.

The mortality is approximately about 15 per cent.

Pathological anatomy. — Beyond evidences of bronchial catarrh, hypostatic pneumonia, enlarged spleen, perisplenitis, patchy reddening of the intestine near the ileo-cæcal valve, injection of the peritoneum, and slight enlargement of the mesenteric and superficial lymphatic glands, no noteworthy lesions have been described.

Ætiology.—The Japanese attribute this disease to the bite of an acarus (locally called *aka mushi*—red insect) resembling the *leptus autumnalis* of Europe. Baelz rejects this idea, but offers no other explanation as to the way in which the virus is

introduced. Men, women, and children are equally susceptible. One attack does not confer immunity, although it appears to render subsequent attacks less severe. Hitherto the virus of the disease, which doubtless enters in the first instance at the site of the primary eschar, has not been discovered.

Treatment.—On the supposition that the disease is introduced by an insect, or through a wound of some sort, care should be exercised by those engaged in hemp culture in the endemic district to protect and keep clean the skin, especially that about the genitals and armpits. There is no specific remedy for the disease; treatment must therefore be conducted on general principles.

NASHA FEVER (NASA, NAKRA).

Drs. Fernandez and Mitra describe (*Trans. First Ind. Med. Cong.*, 1895) under the name of nasha fever, a disease which they say is peculiar to India, and especially prevalent in Bengal. Preceding the fever a peculiar congestion of the mucous membrane of the septum nasi shows itself. Sometimes this congestion is confined to one nostril, sometimes both sides are affected. The pain is insignificant, but the surface of the septum is raised and presents a red and swollen appearance, a circumscribed swelling about the size of a pea (Mitra) being readily recognised. The usual symptoms of fever are present, marked constipation and malaise being very prominent. Frequently headache and pain in the back of the neck, shoulders, and small of the back are urgent. The face appears flushed; there is a feeling of heat and fulness about the head and, according to Fernandez, the pupils are contracted. These symptoms continue from three to five days, when the swelling of the nasal mucosa decreases and the fever subsides spontaneously. The swelling never suppurates. In very rare cases sudden subsidence of the swelling is followed by grave symptoms—high fever, delirium, coma, and death.

One attack predisposes to another, the attacks

appearing at more or less definite intervals of a month, a fortnight, or a week. Both sexes are liable, but females suffer less frequently than males. Children are never attacked; after fifty the disease does not occur. Nasha fever is most prevalent between April and August, being seldom seen during the winter months.

In the discussion which followed the reading of Drs. Fernandez and Mitra's papers at the Indian Medical Congress, Drs. Roy and Bose refused to recognise nasha fever as a special disease, believing that the congestion of the nasal mucosa was a common occurrence in many febrile diseases in India.

Treatment.—In milder cases a saline purgative suffices. Pricking the swelling in the nostril by a needle, or puncture with a lancet, quickly relieves the congestion and fever. Injections of cold water, or of some mild astringent, into the nostrils two or three times a day are said to be useful.

KALA-AZAR.

Kala-azar (black fever) is the name applied to an ill-defined and very deadly disease prevalent of late years in Assam, in the low-lying malarious district between the Brahmaputra and the foot of the Garo hills in the Gaolpara district. Commencing somewhere about 1887, according to Rogers (*Brit. Med. Jour.*, June 5th, 1897), in Bengal, in the Rungpore district, it crossed the Brahmaputra into Assam, where it has gradually extended its area, depopulating whole villages in its gradual but steady advance, and seriously augmenting the mortality and interfering with the material progress of the country.

According to Giles, who was commissioned by the local government to investigate the subject, kala-azar is a slow wasting disease, characterised by great and progressive debility; occasional, though rarely severe, intercurrent attacks of fever; enlargement of the spleen; darkening of the complexion; and, at the end, various dropsical affections. Extreme anæmia is a

constant symptom. Unless during the transient fevers, the body temperature is persistently and markedly sub-normal. The intercurrent fever and the enlargement of the spleen he does not regard as essential features, but rather as accidental malarial complications, and such as are to be expected in the course of any debilitating sickness in a country so notoriously malarious. The darkening of the skin—from which, presumably, the disease takes its name—he attributes to the leaden tint of anæmia enhanced by accumulations of dirt on the unwashed and naturally dark skin of the native. Giles found the ova of the ankylostomum duodenale in the fæces of practically all the cases he investigated. Influenced by this circumstance, and by the anæmia which was so marked a symptom in all, he regarded kala-azar as being merely a severe form of ankylostomiasis.

Rogers, on the other hand, after correctly pointing out that the ankylostomum is exceedingly prevalent in many districts of India in which kala-azar is unknown, opposes Giles's views, and maintains that it is but a form of malaria indistinguishable in its early stage from ordinary malaria. He found the malaria parasite a constant feature in the blood of his patients, and always encountered, *post-mortem*, marked malarial pigmentation of the liver, spleen and kidneys. Rogers further asserts that kala-azar is invariably introduced into hitherto unaffected villages by someone who had contracted the fever in an infected village; the first two or three cases, he says, occur in the same house in which the patient has come to live. He further states that the plasmodium of the kala-azar type of malaria, being of a nature much more virulent than that of the ordinary fevers of Assam, causes a marked cachexia in about as many months as the ordinary fever parasite does in as many years. He also considers that the germ, by intensification, has acquired infective properties, and is capable of passing directly from the sick to the sound through the air or through the soil. It is difficult to understand, however, how so

important a biological revolution could be effected in the habits of the plasmodium.

Other writers agree with Giles in denying the malarial nature of kala-azar. Gibbons, for example (*Ind. Med. Gaz.*, January, 1890), describes the *post-mortem* examination of a case, and states explicitly that there was no pigmentation of the spleen.

It is evident that much clinical, ætiological, and pathological work has yet to be devoted to the study of kala-azar before its true nature can be definitely affirmed. Certain it is that it has no relationship to beriberi, as at one time was asserted.

TYPHOID FEVER IN THE TROPICS.

The existence of typhoid fever in the tropics was for long not only ignored but actually denied, even by physicians and pathologists of repute. Formerly, the idea of malaria so dominated all views of tropical fevers that nearly every case of pyrexia, other than those of the most ephemeral description, or those associated with the exanthemata or with manifest inflammation, was relegated to this cause. When ulceration of the ileum was encountered in the *post-mortem* room, the intestinal lesion was regarded not as the specific lesion of the fever but merely as a complication. More correct views prevail at the present day, and typhoid now ranks not only as a common disease in the tropics but, to the European there, as one of the most commonly fatal. Little is known about typhoid as a disease of natives, beyond the fact that it does attack them; as a disease of Europeans it is only too familiar to the army surgeon in India and to the civil practitioner in most, if not in all, parts of the tropical world.

Typhoid fever is, one might almost say, alarmingly prevalent among young soldiers and civilians in the East. It is very common among them during the first two or three years after their arrival. Fortunately, the liability decreases with length of residence. Apparently a sort of acclimatisation, or rather habituation,

to the poison is established with time, just as tends to be the case with other organic poisons. It is not unlikely that the relative exemption of the native races is owing to a similar immunising effect produced by living in constant contact with typhoid and similar toxic agents. On visiting native cities—Chinese cities, for example—one is filled with amazement at the state of filth in which the people live, and not only live but thrive. The streets are narrow and never cleansed; the common sewer lies beneath the flagstones paving the streets, and through the interstices between the stones can be seen the black, stinking slush in the sewer. The sewerage is not confined in a well-laid cemented drain, but it soaks through the loosely laid, uncemented stones, and thoroughly saturates the ground on which the tumble-down, overcrowded houses are built. Night soil is allowed to remain in wooden buckets inside the houses awaiting collection by the soil merchant who sells it to the market gardener and the farmer. Urine is accumulated in earthenware jars, and is similarly disposed of. The houses are rarely swept and cleaned, hardly ever repaired. In every corner are filth and rubbish. And yet, in such circumstances—circumstances in which the sanitarian would prophesy typhus and typhoid, the population seems to thrive. Doubtless, where the European would almost surely contract typhoid and other filth diseases, the natives have obtained an immunity by habituation. In Japan the privies are inside the house, under the same roof as the dwelling-rooms, and the whole house is generally pervaded by a peculiar, mawkish, privy odour. The natives do not appear to suffer much from this; but I used to see many cases of typhoid in "globe-trotters" who, after visiting Japan, had come to Hong Kong with unequivocal symptoms of this disease. In China, in Japan, and in India little or no care is taken to prevent contamination of the wells with sewage matter, and unless foreigners are very careful about boiling their drinking water and avoiding bazaar-made drinks,

they are almost sure, sooner or later, to be victimised. Typhoid is common also in Cochin China, in the Malay country, in Mauritius, in Africa; the French have had large experience of it in Algeria and their West African possessions; the English have had similar experience in South Africa. It is also found in the West Indies—in fact, everywhere where it has been properly looked for.

It would appear that not only is typhoid a common disease in the tropics, but that it is also a very virulent one, with a death-rate twice as heavy as the death-rate of typhoid in England. According to my experience in China, not only is the tropical form grave from the outset but it is extremely liable to relapse. In England the death-rate is put down at about one in five or six attacked; but in India the elaborate and carefully prepared statistics show a death-rate rather over one in three. What with its frequency and its high rate of mortality, typhoid in India kills more European soldiers than cholera.

Besides exhibiting increased virulence, experience has shown that as against typhoid those sanitary safeguards which are found to be practically sufficient in England are by no means so effective in India. It would also appear that soldiers on the march contract the disease in passing through uninhabited country, in spite of the fact that the camp may be pitched in spots which, presumably, have never been occupied by man before; and although the men may have drunk only of water from springs and streams that were beyond suspicion of fæcal contamination. Similar testimony comes from Australia, where typhoid has occurred in the back country in lonely spots, hundreds of miles from fixed human habitations. From these data the inference is suggested that Eberth's bacillus—assuming it to be the germ of typhoid—under certain conditions of soil and temperature may be possessed of the power to exist as a pure yet virulent saprophyte, for which an occasional passage through the human body is by no means necessary.

It is not requisite to enter further into the subject of typhoid fever, for although, as I stated, this important disease is abundantly common in the tropics, it is not properly classifiable as a tropical disease; moreover, it is fully dealt with in every text-book on general medicine. It is alluded to here more by way of warning the practitioner in the tropics against overlooking it, and against assuming that every case of fever he may encounter is malarial.

TYPHO-MALARIAL FEVER.

Some years ago a good deal was written and said, particularly by American physicians, about what is called "typho-malarial fever." An idea got abroad —and still exists, apparently—that there is a specific disease which, though resembling both, is neither typhoid, nor malarial, nor any of the other recognised forms of continued fever. There can be little doubt that in warm climates, besides the known fevers, there are several, if not many, undifferentiated specific fevers. But the particular clinical group indicated by the term "typho-malarial" is not one of these; for typho-malarial fever is but an ordinary typhoid occurring in an individual who has been exposed to malarial influences; in other words, who has become infected by the plasmodium malariæ.

It has already been pointed out that the malaria germ may remain dormant for months or even years in the body, and then, on the occurrence of severe physiological strain—such as a chill, shock, excessive fatigue, and so forth, wake up again, as it were, and once more multiply and flourish in the blood and give rise to the phenomena of malarial fever. It is a recognised clinical fact, one familiar to our predecessors and much insisted on by them, that any disease process occurring in a person who has once had malarial fever is prone to take on an intermittent or periodic character; as if the previous malarial infection had left a sort of impress of periodicity on the constitution. Doubtless this is owing to the fact that

in individuals with Laveran's parasite dormant in their tissues, the physiological strain implied by the presence of active disease paralyses for the time being the self-protective power, and the plasmodium is once more permitted to multiply and work its mischief in the blood. There are few more depressing influences than typhoid. Little wonder, then, that typhoid in a malarial is often accompanied by clinical evidences of a resuscitation of the plasmodium. And so it comes to pass that an attack of typhoid in malarial countries, or in persons returned from malarial countries, is prone to assume some of the characters of intermittent or remittent fever.

Not infrequently, instead of the slowly increasing headache, malaise, creeping cold, anorexia, and day by day ladder-like rise of temperature, the first sign of typhoid in such circumstances is a violent rigor, immediately followed by rapid rise of temperature which, in an hour or two, mounts to 104° or 105°, to be succeeded in a few hours by profuse sweating and a partial remission of fever exactly resembling an attack of ague. For the next two or three days these attacks are repeated, the remission becoming less complete each time. Quinine may be given but, although the rigors and marked oscillations of temperature are checked, the practitioner is surprised and disappointed to find that the temperature keeps permanently high, and that the typhoid state is gradually developed. Or it may be that a typhoid fever begins in the usual insidious way, runs its usual course for a week or two, and then, in the middle of what is regarded as an ordinary typhoid, rigors and temperature oscillations and other malarial manifestations show themselves. If quinine is given, these oscillations cease and the typhoid resumes its usual course. Or it may be that it is not until the end of the fever and during convalescence that these malarial symptoms are developed. I am not aware of any observations on the blood in typhoid commencing with malarial manifestations, but in an issue of the Boston *Medical and Surgical*

Journal (Vol. cxxxii., No. 6, Feb. 7, 1895) Dr. F. A. Rogers records a case of typhoid in which chill occurred on the twelfth day, followed by quotidian fluctuations of temperature and profuse sweating In this case the plasmodium was found in the blood in abundance. On the administration of quinine the malarial signs subsided, the plasmodium disappeared from the blood, and the typhoid fever ran its course to convalescence in the usual way

The **diagnosis** between typhoid and some forms of malarial remittent is often exceedingly difficult, in certain cases almost impossible, without the assistance of the microscope. The principal points to be kept in view are, first, the mode of incidence of the disease. In typhoid there is a gradual rise of temperature, a daily gain of a degree or so during several days, the maximum not being attained for five or six days; as against the sharp rigor and sudden rise of temperature through five or six degrees in the first twenty four hours in malarial fever. Secondly, the character of the gastric symptoms differ. Thus there is bilious vomiting and perhaps bilious diarrhœa, tenderness of the liver, epigastrium and spleen, and an icteric tint of skin and scleræ in malarial remittent; in contrast to the abdominal distension, perhaps, the iliac tenderness and gurgling, and the peasoup stools of typhoid. Such signs as epistaxis, deafness, and cheek flushing in typhoid have a certain weight, but skin eruptions in the tropics are of little aid in the diagnosis of such cases. Prickly heat, or its remains, is present in nearly everyone, sick and healthy, malarial or typhoid patient alike; so that rose spots are to be found in nearly all fevers in hot weather. None of these signs can be considered as absolutely diagnostic; all or any of them may be present in typhoid, and all or any of them may be present in malarial remittent. The only really diagnostic marks are tertian periodicity, amenability to quinine, and, above all, that supplied by the plasmodium malariæ and the Widal serum test. In all doubtful cases the plasmodium

should be sought for; if it is found, the case has certainly a malarial element, and quinine is indicated. If it is not found, and if quinine has not been administered and several negative examinations of the blood have been made, and if the observer has confidence in his skill as a microscopist, the chances are the case is one of pure typhoid. Nevertheless, if the plasmodium is found typhoid is not necessarily excluded, for the case may be one of typhoid in a malarial, that is typho-malarial fever.

Prognosis and management.—Remittents under suitable treatment we expect to see recover; typhoids too often go the other way. A word of caution may be given about these tropical fevers of doubtful character. The caution has reference to prognosis and treatment. In forming diagnosis too much weight must not be attached to the presence or absence of diarrhœa; constipation is much more common in tropical typhoid than in the disease in Europe. Diagnosis, therefore, must not be too much influenced by absence of diarrhœa, and the practitioner must not be led by the presence of constipation into giving active purgatives. Purgatives are often of the greatest service in malarial remittent; but if, in consequence of a mistake in diagnosis, it is assumed that a case of typhoid is remittent, and large doses of calomel and other cathartics are administered, the result may be disastrous. If doubt exists about diagnosis, and quinine is given, it will not do a typhoid much harm. It is a good rule, therefore, when in doubt to give quinine, but to avoid purgatives.

CHAPTER XII.

HEAT-STROKE.

THE term "heat-stroke" conveys the suggestion that heat is the leading ætiological factor in the various morbid conditions which custom has grouped under this and similar names.

Until irrefutable evidence has clearly demonstrated the true cause of any given disease, it is a very grave error to base the name of such disease on some crude hypothetical ætiological conception. Such a nomenclature is sure to lead to confusion, to mistakes in practice, and to retard progress. There is no better illustration of the truth of this remark than that supplied by the group of diseases under consideration.

The expression "heat-stroke" covers several distinct, one might say of two of them almost opposite, clinical conditions. One of these is *heat-exhaustion*, virtually a syncope, which may occur anywhere and in any climate, high atmospheric temperature, whether natural or artificial, being its essential ætiological factor. The other, of which hyperpyrexia is the most striking clinical feature, is a well-defined and possibly specific fever, having a peculiar endemicity and assuming at times in the endemic area almost epidemic characters. Like yellow fever, dengue, tropical elephantiasis and other tropical diseases, this second form of heat-stroke occurs only in conditions of high atmospheric temperature; but, as with these diseases, it by no means follows that though occurring in high temperature, it is caused by high temperature. To obviate confusion, and following the excellent example of Dr. L. Sambon (*Brit. Med. Journ.*, March 19, 1898), I shall describe this disease under its ancient name *Siriasis*.

Besides these two well-defined morbid states associated with high atmospheric temperatures, there is another, but ill-defined, group of heat-stroke cases which, to all appearance, result exclusively from exposure to the direct rays of the sun. These cases might be classified under the term *Sun-traumatism.*

Although not all of them strictly classifiable as fevers, in deference to custom and for convenience I shall describe these three phases of so-called "heat-stroke" in this place and as a group.

HEAT-EXHAUSTION.

Definition.— Sudden faintness, or fainting, brought about by exposure to high atmospheric temperature.

Ætiology.—The healthy human body when untrammelled by unsuitable clothing, when not exhausted by fatigue or excesses, when not clogged by surfeit of food, by alcoholic drinks or by drugs, can support with impunity very high atmospheric temperatures. In many parts of the world men live and work out of doors in temperatures of 100° or even of 120°. Many industries are carried on at temperatures far above this; glass blowing, sugar-boiling, for example. The stokers of steamers, especially in the tropics, discharge for hours their arduous duties in a temperature often over 150° F.

When, however, the physiological activities have become impaired by disease, especially by heart disease, kidney, liver or brain disease, by malaria, by alcoholic or other excesses, by fatigue, by living in overcrowded rooms; or when the body is oppressed by unsuitable clothing; or in the presence of a combination of some of these, then high atmospheric temperatures are badly supported, the innervation of the heart may fail and syncope may ensue. Chevers, than whom few have had better opportunities of forming a sound opinion, speaking of this subject, says: "Numerous as the constitutional causes of heat-stroke are, all Indian experience

combines to show that drunkenness is the chief." The tropical practitioner will do well to bear this remark in mind; it applies not only to heat-exhaustion, but also to all forms of disease grouped under the term "heat-stroke."

Heat-exhaustion, then, is one form of what, when the subject of it happens at the time to be exposed to the sun, is called "sun-stroke," or when the patient happens to be at the time under cover is called "heat-stroke." In nine cases out of ten this sun-stroke, or heat-stroke, simply means syncope; syncope caused by solar or atmospheric heat, or a combination of these, acting on a body whose resistance has been impaired by disease, or by trying unphysiological conditions. This form of heat-stroke, consequently, has no special geographical distribution and no special morbid anatomy or pathology. For obvious reasons it is most apt to occur in warm weather, and in tropical climates; and on this account its recognition, prevention, and treatment, have special claims on the student of tropical medicine.

Symptoms.—When attacked with heat-exhaustion the patient feels giddy, and perhaps staggers and falls. He is pale, his pulse is small, soft, and perhaps fluttering; his breathing shallow, perhaps sighing, never stertorous; his pupils are dilated; his skin is cold; his temperature is sub-normal; and he may be partially, more rarely wholly, unconscious. Usually, after a short time he gradually recovers; very likely with a splitting headache and feelings of intense prostration. In a small proportion of cases the faint is not recovered from, and death ensues.

Treatment.—In syncopal heat-stroke the patient should be laid at once on his back in a cool, airy, and shaded place. His clothes should be loosened, a little water dashed on his face and chest, and ammonia held to his nostrils. If necessary, a stimulant may be given by the mouth, or injected into the rectum or hypodermically. It is a mistake to douche these

cases too freely. The object is rather to stimulate than to depress.

SUN-TRAUMATISM.

There is a large, ill-defined, and difficult-to-define class of heat-stroke cases which belong neither to the category of heat-exhaustion, nor to the very definite and probably specific disease described under the name siriasis. The morbid phenomena in this class of sun-induced disease are attributable, apparently, to a peculiar physical action of the direct rays of the sun on the tissues. To this category belong, it seems to me, those sudden deaths occurring without warning during, and manifestly in consequence of, exposure to the sun. Such may have been the sudden deaths described by Parkes, Maclean, Fayrer, and others, in which soldiers in the excitement and stress of battle, and while oppressed with thick clothing and heavy accoutrements and exposed to a blazing sun, suddenly fell forward on their faces and, after a few convulsive gasps, died. In these instantaneously fatal cases the paralysis of the heart or respiration seems to be more of the nature of shock as from a blow or other sudden and violent impression on the encephalon.

Doubtless, indeed it is a well-known fact, the strain undergone in these and similar circumstances may cause an apoplexy or rupture of some description in tissues prepared for such a cataclysm by morbid degenerations of long standing.

Besides these there is another type of case in which, after prolonged exposure to the sun, a febrile condition is established. This is sometimes of great severity, and may be characterised by intense headache, a rapid full pulse, a pungent dry skin, intolerance of light, sound and movement, and occasionally by vomiting. This condition suggests meningeal congestion, possibly inflammation. The acute phase may be quickly recovered from, or it may prove very persistent and last for days or weeks. It may

leave no injurious effects, or it may be followed by a variety of morbid nervous phenomena which may be transient, or which may be of a more permanent character Among the distressing sequelæ authors have mentioned tremor, loss of memory, amaurosis, deafness, various paretic conditions, epilepsy, insanity, persistent headache, recurring headache, dyspeptic conditions, sensitiveness to heat and especially to exposure to the sun. How far these sequelæ are entirely attributable to sun exposure, or how far they depend on independent diseases, as syphilis, for example, the local cerebral manifestation of which many have been provoked, though not actually caused, by the sun-traumatism, it is not always easy to say.

The morbid anatomy, as well as the clinical symptoms, indicate meningitis as a feature in these instances of reputed sun traumatism Authors refer to thickenings and opacities of the meninges, and even to thickening and roughening of the calvarium.

Many speculations have been advanced as to the pathogenesis. Manifestly it is not altogether, if at all, a question of caloric, for such effects do not result from exposure to the heat of a furnace, however intense. There appears to be some special element in the solar spectrum capable of injuriously affecting the tissues, particularly if they have not become gradually habituated to sun exposure. That some such element does exist is proved by the phenomena of sun erythema, of that form of skin pigmentation known as sun burning, and, possibly, of leucodermia. The sensation of distress brought on by exposure to a hot sun, which is quite a different sensation from that produced by the heat of a fire, points in the same direction. In this connection we are forcibly reminded of the phenomena of the Routgen rays and of their effects on the tissues.

Treatment. Patients suffering from sun traumatism must be kept as quiet as possible in a cool, airy, and darkened room For a time the head should be kept shaved and cold applied to the scalp. The

bowels must be free, food light and unstimulating, and alcohol in every form strictly forbidden. Restlessness and insomnia are best treated by the bromides. For a considerable time the patient will be conscious of loss of memory and feebleness of intellectual power and of the faculty of concentration. He may be irritable, liable to headache, and extremely sensitive to heat—more particularly the heat and glare of the sun. So soon as he is able to be moved he must be sent to a cold climate, and there remain until all trace of his illness has completely disappeared. Indeed, it is questionable if the subject of pronounced sun-trauma should ever again risk the dangers of a tropical climate; certain it is that he should not return to the tropics so long as the slightest evidence of cerebral trouble remains.

For persistent headache and other signs of chronic meningitis, courses of the iodides and bromides, repeated blistering of the neck and scalp, together with careful dieting and general hygiene, should be tried. In not a few instances, in spite of the most careful treatment, medicinal and climatic, serious permanent disease of the encephalon remains, giving rise to various and often incurable troubles, and, very commonly, to distressing intellectual enfeeblement.

SIRIASIS.

Definition.—An acute disease developing in the presence of high atmospheric temperature, and characterised by hyperpyrexia, coma and extreme pulmonary congestion.

Nomenclature.—This is, perhaps, the most important of the several diseases covered by those loosely used terms, sun-stroke, heat-stroke, *coup de soleil*, insolation, heat-apoplexy, heat-asphyxia, thermic fever, and so forth. As stated, I have followed Dr. Sambon in adopting the name Siriasis, because this term, whilst it is distinctive, embodies no ætiological theory; it has the further merit of being the most ancient of the many names applied to the disease.

The geographical distribution of siriasis,

like that of yellow fever, appears to be remarkably restricted. It is true that this type, or what passes for this type of disease, has been reported as occurring in many countries. On careful examination, however, it will be found that a large proportion of the reputed cases are really examples of other diseases, more especially of cerebro-spinal fever, apoplexy, tubercular meningitis, delirium tremens, pernicious malaria, or some other phase of acute disease, but not of true siriasis. According to Sambon, hyperpyrexial heat-stroke is rigidly confined to certain low-lying, sea-coast districts, and to the valleys of certain rivers. It is never found in high lands, nor above a relatively low altitude—600 feet.

It is unknown in Europe. The endemic areas are:—in America, the east coast littoral of the United States, more especially in the great towns; the Mississippi valley; the coast of the Gulf of Mexico; the valleys of the Amazon, and of the La Plata; and the South Atlantic coast. In Africa, the valley of the Nile; the coasts of the Red Sea; and a low-lying part of Algeria, near Biskra. In Asia, Syria; the valleys of the Indus and Ganges; Lower Burma; Tonquin; and south-east China. In Australia, the Murray River district; the Queensland coast; and, possibly, the plains of Sydney. No doubt, it occurs elsewhere in corresponding meteorological and telluric conditions; but, undoubtedly, many large areas in the tropical world, and especially so the interior of continents, are exempt from siriasis. It is not met with on the high seas, although it is well known on ships in the narrow land-locked Red Sea and Persian Gulf.

Ætiology.—Newcomers to the endemic areas and Europeans are more liable than natives or long residents. Apparently, long residence confers a relative immunity, although not an absolute exemption.

All ages and both sexes are susceptible; but, in consequence of their habits and more frequent exposure to the predisposing and immediate causes, men are more liable to siriasis than are women.

Predisposing influences, similar to those in heat syncope and sun-traumatism, powerfully influence the liability to siriasis. Amongst these are all physiological depressants; notably intemperance, fatigue, overcrowding, unsuitable clothing, malaria, acute disease, and also chronic organic diseases of the important viscera.

Siriasis has generally been attributed to a direct action of atmospheric or solar heat on the body. Many theories of the *modus operandi* of this assumed cause have been advanced. Among these may be mentioned superheating of the blood by the high temperature of the surrounding atmosphere; paralysis of the thermic centres causing (*a*) over-production of heat, or (*b*) retention of body heat; pressure on the brain by expansion from heat of the cerebro-spinal fluid; vaso-motor paresis; paresis of the heart ganglia; excess of carbonic acid in the blood; coagulation of myosin; suppression of sweat; deficient serosity of the blood from excessive sweating, and so forth.

It is well known that neither high atmospheric temperature *per se*, nor high bodily temperature, unless the latter be associated with some special toxin, gives rise to symptoms at all like those of siriasis. Considering these two facts, and at the same time the peculiar and capricious distribution of the disease, the circumstance that its prevalence curve does not always correspond with the atmospheric temperature curve; that the degree of prevalence varies in the endemic area from year to year; that it is not most prevalent in the hottest years, seasons, or places; that it becomes epidemic at times; that it runs a definite course; that it may relapse; that in many instances it has definite premonitory symptoms; that it has peculiar lesions; and that it tends to terminate by crisis, in other words, that it behaves like pneumonia or any other specific fever, Sambon has boldly asserted that siriasis is a germ disease, like yellow fever or dengue, and, like these, is caused by some organism which demands for its

Different writers mention a variety of what may be described as minor symptoms. These vary in different cases, and are by no means always present or characteristic; but in siriasis the essential symptoms, high fever and profound nervous disturbance, generally associated with insensibility, are invariably present.

Unless active measures to lower temperature are taken early in the progress of the case, and unless these measures are vigorously carried out, in the great majority of instances death occurs within a few hours, or even minutes, of the onset of insensibility. The immediate cause of death is generally the failure of respiration. Rarely do cases linger for a day or two. Partial recovery is sometimes followed by relapse. In favourable cases the disease usually terminates by crisis, and convalescence is rapid.

Mortality. As might be supposed, some types of heat-stroke are much more dangerous than others; siriasis infinitely more so than ordinary heat exhaustion. Treatment, if early instituted and judiciously carried out, has undoubtedly a powerful influence in reducing mortality. Taking one type of heat-stroke with another, the case mortality among English troops in India is about one in four; in the year 1892, of 223 European soldiers admitted to hospital for heat-stroke, 61 died.

Morbid anatomy.—A notable feature is the early appearance of rigor mortis. The blood is remarkably fluid, or but feebly clotted. The venous system is gorged, the dark fluid blood pouring from the phenomenally engorged lungs and other viscera on section. Both blood and muscles are said to yield an acid reaction more or less pronounced. The red blood corpuscles are crenated, and do not form rouleaux. If the *post-mortem* examination is made shortly after death and before decomposition changes have set in, the heart, particularly the left ventricle, is found to be remarkably rigid; this rigidity is sometimes described as being of woodeny hardness.

If the examination be made at a later period, the muscle of the heart will be found soft and flabby. There may be some venous congestion of the meninges of the brain, but the brain itself shows no important vascular changes. The intestinal mucosa, as well as that of the stomach, is swollen and exhibits patches of congestion.

Pathology.—As may be gathered from the remarks on ætiology, the pathology of siriasis, so far, is in a very unsettled state, and will continue to be so until the essential cause of the disease has been finally determined.

Diagnosis. — The presence of high fever is sufficient to differentiate siriasis from sudden insensibility caused by uræmia, by diabetic coma, by alcoholic and opium poisoning, and by all similar toxic conditions. Cerebral hæmorrhage, particularly pontine, may, after some hours, be followed by high temperature; but here the febrile condition follows the insensibility, whereas in heat-stroke the febrile condition precedes the insensibility. The diagnosis from a cerebral malarial attack may be very difficult; chief reliance has to be placed on the history, if obtainable, on the condition of the spleen, and, especially, on the result of microscopic examination of the blood. Malarial fevers and the early stages of the eruptive fevers in children are very apt to be regarded as heat-stroke, particularly if there has been recent exposure to a hot sun. Cerebro-spinal fever, so often mistaken for siriasis, may be recognised by the occipital retraction, the irregular pupils, the frequent occurrence of strabismus, the comparatively low and fluctuating temperature, the associated herpes, the initial rigor, and its long duration.

Treatment.—In all fulminating fevers, including siriasis, occurring in warm climates, if malaria be suspected, particularly if the plasmodium be discovered in the blood, quinine should be injected hypodermically at once—seven grains or so of the hydrochlorate; this dose should be repeated three or four times at intervals

of four hours. In every case of siriasis, whether it has been deemed advisable to administer quinine or not, attention must at once be given to reduce temperature by such rapidly-acting measures as the cold bath, or ice applied in various ways to the head and body. Antipyrin, antifebrin, and all other antipyretic drugs are of very little service, even if, in consequence of their depressing action on the heart, they be not actually dangerous; in all serious cases of siriasis, these drugs must be carefully avoided. Chandler (New York *Med. Rec.*, June 5, 1897), speaking from an experience of 197 cases in which the mortality amounted only to twelve, gives some excellent directions for the management of hyperpyrexial cases. He directs that the patient be placed undressed on a stretcher, the head end of which is raised slightly so as to facilitate the escape of involuntary evacuations and to provide for drainage. A thermometer is kept in the rectum. The body is covered with a sheet upon which are laid numerous small pieces of ice, larger pieces being closely packed about the head. Iced water is then allowed to drip for thirty or forty minutes on the patient from drippers hung at an elevation of from five to ten feet. A fine stream of iced water poured on the forehead from an elevation will act as a stimulant and rouser; this is a very powerful measure, and must not be kept up for longer than one or two minutes. A hypodermic injection of forty minims of tincture of digitalis is given as soon as possible, its administration being preceded in the case of plethoric patients showing much arterial tension (but not otherwise) by a small bleeding. The application of cold should be at once discontinued in hyperpyrexial cases so soon as the thermometer in the rectum has sunk to 104°; and in cases of simple thermic fever, in which the temperature has not exceeded 106°, when it has fallen to 102°. If these powerful antipyretic measures are carried beyond this point the fall of temperature may continue below the

normal, even to as low as 91°, and dangerous collapse ensue. On discontinuing the iced sheet, the patient should be wrapped in a blanket, and hot bottles applied to limbs and trunk. Very likely perspiration, a very favourable sign, will then set in. Stimulants may now be necessary. Strychnine, owing to the marked tendency to convulsions present in heat-stroke, must on no account be used as a cardiac stimulant. Convulsions are best controlled by cautious chloroform inhalations. As death in heat-stroke generally results from failure of respiration, Chandler strongly recommends artificial respiration when the breathing threatens to become suspended; he claims to have obtained some marvellous results from this expedient. It should be kept up for half an hour or longer.

During convalescence, great care must be exercised to shield the patient from all influences calculated to provoke relapse.

PREVENTION OF HEAT-STROKE.

In heat-stroke climates great attention should be paid to the general health; if this be not satisfactory, exposure to the sun and to high temperatures must, so far as possible, be avoided. Alcoholic drinks, gluttony, excess of animal food, too much tobacco smoking, in fact, dissipation of all sorts, are especially to be deprecated. Individuals suffering from malarial or other fevers, or from chronic liver or kidney disease, run great risk if they are careless about exposing themselves to the sun. Violent exercise, excessive fatigue, want of sleep, constipation, are also to be avoided.

Clothing ought to be light and loose fitting, the under-garment being of thin woollen material. In going out in the sun the head must be protected by a wide-brimmed pith hat, protecting the temples and neck as well as the top of the head. This hat should be so constructed as to admit of free ventilation around the head. A pad of cotton sewn into the back of the

coat in such a way as to protect the spine is a wise measure, and one adopted by experienced sportsmen in India. The phenomena connected with the Röntgen rays suggest the possibility that there may be solar rays, other than the ordinary heat rays, which, although they may be able to pass through organic materials, can nevertheless be arrested by metals. If this be true for the sun as well as for the electric spark, a useful addition to the sun hat would be a thin plate of some light metal placed between the layers of pith constituting the basis of the ordinary solar topee. A sheet of tinfoil or other light metal would not perceptibly add to the weight of the head-gear. A white umbrella, lined with green, ought never to be despised. Tinted (smoke colour) goggles are probably a protection, as they certainly are a great comfort in mitigating solar glare.

Rooms should be kept dark during the day, and cooled by means of punkahs, thermantidotes, tatties, venetians, and other contrivances. In barracks and ships there must be no overcrowding. In very hot weather European soldiers should, if possible, sleep under punkahs. Military drills should be reduced to a minimum, and take place in the cool of the morning only, and after the soldier has had a cup of tea or coffee and some light food. Marches should be short, interrupted by frequent halts, and be got through if possible in the early morning. While marching the men ought to be in open order, relieved of all unnecessary weights, and be well supplied with water. Camps should be pitched in spots as cool and airy as may be available and, when practicable, on turf and under large spreading trees free from undergrowth. Double canvas, and grass or boughs laid on the wall of the tent, will do much to mitigate the temperature within.

CHAPTER XIII.

UNCLASSED FEVERS OF THE TROPICS.

THERE can be little doubt that in the tropics there are a number of fevers specifically distinct from any of the foregoing, and also from the better-known fevers of temperate climates. Such fevers are constantly met with and are a perpetual puzzle to the conscientious diagnostician. Up to the present little, if anything, of a truly scientific character has been done towards describing, separating, and classifying them. Some attempts have been made to arrange these imperfectly differentiated fevers on a clinical basis; but, until their causes have been discovered and, above all, until they have been studied in reference to any possible connection they may have with the plasmodium malariæ, anything like a sound classification and description has to be postponed. So far as known, they are not associated with distinctive exanthems or even with distinctive visceral lesions; a circumstance which has contributed, doubtless, to retard our knowledge in a very important department of tropical medicine. Another circumstance which has retarded progress in this matter is the unscientific classification of fevers adopted by our military medical authorities, and to which military medical officers have been obliged, or have elected, in great measure to conform. It would seem that every case of fever of short duration, as well as those cases which show an intermittent character, have to appear in the Army Returns as "ague." This misleading, slovenly, not to say dangerous, practice, must have had a powerful influence in retarding the study of the pyretology of

the tropics, at all events by our principal medical pioneers there —the army surgeons.

Recently, Crombie (*Trans. First Ind. Med. Cong.*) has attempted a classification of these fevers on a clinical basis, which, so far as it goes, is of distinct value. His remarks apply solely to the fevers of India; but I can recognise in his descriptions clinical forms which I frequently met with formerly in China. It is fair to infer from this latter circumstance that, if these fevers are found in India and China, they probably occur in other warm countries.

Crombie divides them into **simple continued fever, low fever**, and **non-malarial remittent.** To these I would add yet another which, from experience in China, I regard as a distinct clinical entity, and which from its peculiar feature I would call **double continued fever.**

Simple continued fever. Simple continued fever generally, if not invariably, commences with a rigor, the temperature rapidly or more slowly mounting to 104°, 105°, or even 106° There is headache, malaise, a white furred tongue, anorexia, thirst, and perhaps vomiting The fever lasts usually from three to eight days; occasionally it is prolonged for two, three, or four weeks. Crombie remarks that these cases are particularly common in towns, and are known locally as Bombay fever, Calcutta fever, and so forth. It might be suggested that such fevers are mild or aborted typhoid; but in the complete absence of the characteristics of enteric, the insignificant mortality, and the absence of complications, so grave a diagnosis does not seem to be justified. It is customary to attribute them to heat, chills, change of season, acclimatisation, irregularities in diet, exposure to the sun, and the like. As to how far these ætiological speculations are correct, it is hard to say.

Low fever. Like the preceding, this type of fever is not an unusual one among Europeans in the tropics. Its characteristics are indefinite duration—weeks or months—a persistent though slight rise of

temperature rarely above 101·5°, but never below 99°, anorexia, debility, loss of flesh, and a tendency to bilious diarrhœa. It is unrelieved by quinine or arsenic; but it almost invariably responds to a change of air, especially to a trip to sea.

Non-malarial remittent. Crombie remarks that it is a pity we have no better name for this fever, which is of very frequent occurrence in India, and is one of the most fatal of the fevers there. Remittent is a misnomer, for the symptoms are even less remitting than those of typhoid. The temperature runs high, touching 104° or 105° for a long part of its course. It begins not unlike simple continued fever. By some it is considered a variety of typhoid, notwithstanding the absence of many of the symptoms of that disease. Hepatic enlargement and congestion are early and constant conditions; but the spleen, as a rule, is not distinctly enlarged.

"Bilious diarrhœa, in no respect resembling the diarrhœa of typhoid, is also a very frequent symptom. Quinine—often given in large and repeated doses in these cases—is not only not useful but so obviously adds to the distress of the patient, without in any way producing an improvement in the progress of the symptoms, that it is very soon abandoned. Meanwhile, the temperature continuing persistently high, marked head symptoms, especially delirium of a muttering and irritable kind, come on, and the patient may even, and often does, pass into a condition of coma from which he can hardly be roused. This condition of persistent high temperature without marked remission, a distinctly enlarged and congested liver, bilious diarrhœa, congestion of the back of both lungs, and a low, muttering delirium, is generally reached by the eighteenth to the twenty fourth day. If coma supervenes, the patient frequently dies about this period. In more favourable cases, where the symptoms are less severe, they may continue for a week or two longer. In such the average duration of the case is six weeks" (Crombie).

Crombie, although he has seen this fever in Europeans, regards it as being essentially a disease of natives. It is uncommon after thirty, but is frequent enough in childhood.

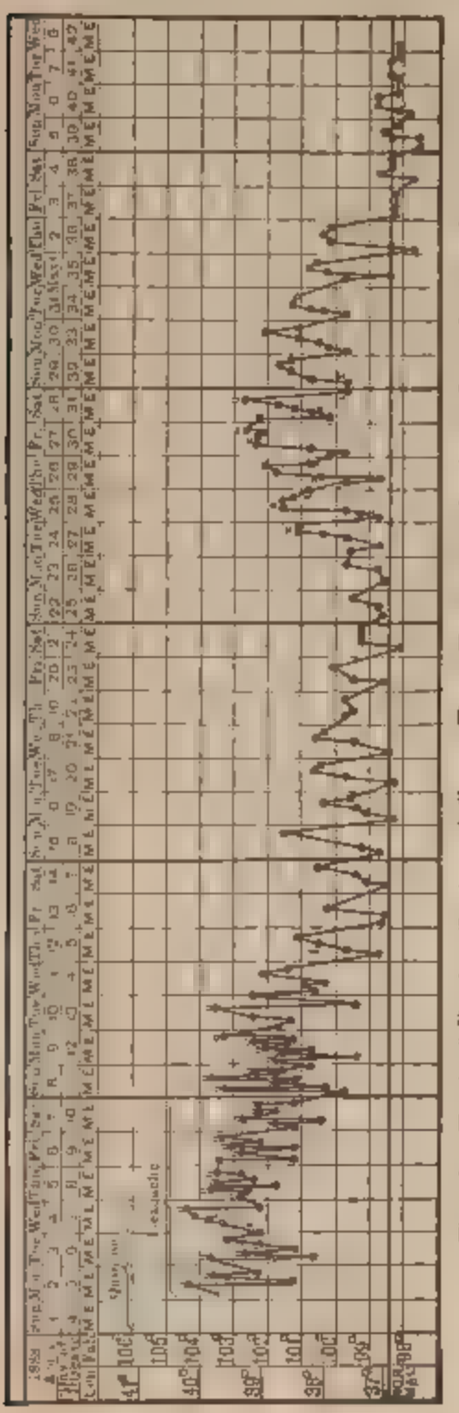

Fig. 23. Chart of Double Continued Fever Hong Kong. o indicates a dose of antipyrin.

Double continued fever.—In South China I encountered, both in Amoy and in Hong Kong, a peculiar type of fever, apparently of little gravity as affecting life, but sufficiently distressing while it lasted. It was characterised by an initial pyrexial stage of from ten days' to a fortnight's duration, followed by a stage of from three to seven days' relative or absolute apyrexia which, in its turn, was succeeded by another spell of about ten days' duration of smart fever, and then by convalescence (Fig. 23). Both in the primary and in the terminal fever the evening temperature may rise to 104° or 104·5°. It might be said that such cases

were relapses of simple continued fever; but as I have, on at least two occasions, seen the same succession of events occurring almost simultaneously in two patients living in the same house—once in husband and wife, and once in brother and sister—it seems probable that this is a special form of disease, and that the double fever is a constant and characteristic feature. In the case of the brother and sister the march of their fevers was strictly simultaneous, the primary fever, the apyretic interval, and the terminal fever occurring in both patients on the same days. Beyond a certain amount of headache and febrile distress there are no special symptoms, so far as I have been able to observe, nor any special complications.

Diagnosis.—The diagnosis of these imperfectly differentiated fevers is always a difficult matter, specially so during their early stages. On the one hand, among other possibilities that of typhoid, and on the other that of malaria, have to be considered. The persistent absence from the blood of the plasmodium and of pigmented leucocytes, if vouched for by an experienced observer, and the negative results attending subsequent administration of quinine, together with the absence of marked periodicity in the symptoms, of pronounced anæmia and of marked enlargement of the spleen, should be decisive against malaria. But, in the present state of our knowledge, it is very hard indeed to exclude typhoid until the case is well advanced. It may be that further experience of the Widal blood test will establish its title to be regarded as an absolutely pathognomonic sign of the presence of Eberth's bacillus. In this event the practitioner will have in his possession an invaluable aid in the diagnosis of tropical fevers. As things are at present, in cases in which there is the slightest doubt it is an excellent rule to regard all doubtful fevers as being possibly typhoid.

Treatment.—It is well at the commencement of doubtful tropical fevers to be as guarded in treatment as in diagnosis, and to eschew active purgatives, to

enjoin rest in bed, to place the patient on a bland, unstimulating fluid diet, and to confine medication to some innocent fever mixture. There is no specific treatment for any of these unclassed fevers. Each case has to be dealt with on its own merits and on general principles. Headache may be relieved by cold applications to the forehead, by an ice cap, or, especially if temperature rises high, by sponging and, if not otherwise contra-indicated, by occasional doses of antipyrin or some similar drug. If quinine, on the supposition that the case is malarial, has been freely tried, and without benefit, it must not be persisted with. As already stated, "low fever" should be treated by change of air, and more especially, where feasible, by a trip to sea.

SECTION II.—GENERAL DISEASES OF UNDETERMINED NATURE.

CHAPTER XIV.

BERIBERI (KAKKE, BARBIERS).

Definition.—Beriberi is a specific form of multiple peripheral neuritis occurring endemically, or as an epidemic, in most tropical and sub-tropical climates, and also, under certain artificial conditions, in more temperate latitudes. The mortality is considerable, sometimes very high, death being usually dependent on heart paresis.

Historical.—The special nature of beriberi was recognised by the Dutch in the early years of their intercourse with the East. Later, it was studied by British physicians in India, particularly by Malcomsen, Carter, Waring, and Morehead. It was not until the widespread epidemic in Brazil, to be alluded to presently, that beriberi began to receive attention from the present generation of medical men; and it was not until Mr. Anderson, of St. Thomas's Hospital and then of Tokio, Japan, Dr. Simmons of Yokohama, and Professors Scheube and Baelz, also of Tokio, took the matter up that it was studied by modern methods, accurately defined, and its pathology correctly apprehended. Scheube and Baelz were the first distinctly to show that beriberi is of the nature of a specific peripheral neuritis similar to that of diphtheria or alcohol, a view which was subsequently confirmed and adopted by Pekelharing and Winkler and by many other observers.

Geographical distribution.—The area of the endemic distribution of beriberi is co-extensive probably with the tropical and sub-tropical belts; doubtless it exists in many places where its presence is not generally suspected. It is the scourge of many of the mines and plantations of the Malay and Eastern Archipelagoes. It is apt to break out among the coolie gangs engaged on extensive engineering works in the tropics, such as the Panama Canal or the Congo railway. It haunts the Dutch army in Sumatra, and used to be common enough, until better hygienic methods prevailed, in the British armies in India. It is at home in many parts of Japan, particularly in her large, low-lying, damp, over-crowded cities. It is prone to break out in jails, in schools, in ships. Sometimes, as an epidemic wave, it passes over a tropical country, as was the case in Brazil in the early 'sixties, where it still lingers. Sometimes sporadic cases crop up here and there; although generally, when it does appear in a place, it attacks large numbers, picking out particular houses and districts. Lately we had an account of a small epidemic among a group of Western Australian natives, and also among Chinese on the eastern seaboard of Australia, a continent where beriberi was formerly supposed not to exist. Similarly, it appeared lately, apparently for the first time, in Fiji. A little while ago I saw a case of beriberi from Lake Nyassa, another from the Upper Congo, another from Hayti. We hear of it also from Havana, from New Caledonia, from the Sandwich Islands—all of them places not before known to be liable to this disease. So that the area is, as I have said, probably a very extensive one. Indeed, within the last few years it would seem that it includes the temperate as well as the tropical zones. Recently beriberi showed itself in a lunatic asylum in Ireland—Richmond Asylum, Dublin—and something like it has been seen in lunatic asylums in the United States, and also among the fishermen on the North American coast.

Symptoms.—Medical visitors to the native hospitals in many parts of the tropical world are likely to have their attention arrested by the large proportion of cases of partial paraplegia, of cases of œdema of the legs, and of cases of general dropsy. These, for the most part, are cases of beriberi.

Fig. 24.—Beriberi (*Bentley*).

Paraplegic cases.—On examining one of the paraplegic cases referred to (Fig. 24), it will be found that, besides paraplegia of greater or lesser degree, there is a certain amount of anæsthesia or of numbness of the skin, particularly of the skin over the front of the tibiæ, the dorsa of the feet, the sides of the thighs, perhaps also of the finger tips, and of one or two areas on the arms and trunk. The visitor may be struck with the thinness of the patients' calves, the flabby state of the gastrocnemii; and by the fact that if, whilst making the examination, he should handle these and the neighbouring muscles somewhat roughly, particularly if he should squeeze them against the underlying bones, the patient will call out in pain and try to drag the limb away. The thigh muscles, likewise, may be found to be similarly tender, and so

may the thenar, the hypothenar, and the arm muscles; like the calf muscles, these too may be wasted and flabby. Very probably there is a loss of fat as well, the panniculus adiposus being everywhere very meagre. If tested electrically, the muscles exhibit to perfection the reaction of degeneration. If the knee reflex be tested in the usual way, after the first week there will be no response whatever; nor can any clonus be elicited. As a rule, all the deep reflexes are lost; but the superficial reflexes, unless in extreme conditions of paresis and muscular atrophy, are usually present and more or less active. If the patient is set to button his jacket or to pick up a pin, possibly he has a difficulty about it, or perhaps he cannot; he may bungle and fumble like an advanced ataxic. There is more than ataxia, however; for the hand grasp is so enfeebled that he may have a difficulty, on this account as well, in holding his rice bowl and feeding himself. There is no tremor of the hands; and very rarely is there any paresis of the ocular muscles, or of the muscles of the face, of mastication, of the tongue, or of the pharynx. The sphincters and bladder operate satisfactorily, and the functions of the alimentary canal are carried on fairly well, although there is often some dyspeptic distension and oppression after food. On the patient being got out of bed and started to walk, if he is able to progress at all his gait will be markedly ataxic; but he is not ataxic merely, for, just as with the hands, it will be seen that, in addition to want of co-ordinating power, there is great muscular weakness. If he is laid on the bed and asked to raise his legs, he is perhaps hardly able to get them off the mat, to cross them, or to place one foot on the top of the other. Very probably he is the subject of marked ankle-drop, so that he drags his toes when he attempts in walking to advance the foot; he has therefore to raise the foot very high, letting it fall on the ground with a flop when he brings it down again. His ataxia and his muscular weakness, as well as the partial anæsthesia from

which he suffers, make him adopt all sorts of devices to assist him in progression (Fig. 25).

Manifestly these patients are suffering from some

Fig. 25.—Beriberi (*Bentley*).

form of peripheral neuritis. But their general health is good for the most part; their tongues are clean, their bowels are fairly regular, and there is nothing amiss with the urine Digestion, assimilation, and excretion go on fairly satisfactorily.

The heart and circulation.—When the heart is examined, if the case be at all recent or moderately severe, attention is at once arrested. On inspection it may be remarked that the impulse is diffuse or is obscured by pericardial effusion: that there is epigastric pulsation: that the carotids throb too violently; that there is that peculiar wobbling, pulsating movement in the jugulars that denotes tricuspid insufficiency. On percussion the praecordial area is generally found to be enlarged, perhaps very greatly enlarged, particularly to the right: and on auscultation loud bruits, usually systolic in rhythm, may be heard. Marked reduplication of the sounds, particularly of the second sound, are to be noted. The auscultator will also be struck by the peculiar spacing of the intervals between the sounds. It may be hardly possible to tell by the ear alone which is the first pause, and which is the second. They seem alike in point of duration: so that the sounds of the heart are, like the beats of a well-hung pendulum clock, evenly spaced, and not, as they are in health, separated by a long and a short interval, like the beats of an ill-hung clock. It will also be observed that the heart is very irritable, becoming easily quickened by exertion. All these signs vary in degree from time to time in the same case, and differ in degree in different cases. It will be judged, therefore, that, in addition to peripheral neuritis, there is serious disease in the circulatory system, particularly in its innervation: that there is a dilatation of the right side of the heart: and that there is a state of relaxed arterial tension.

Dropsical cases.—In the next bed, perhaps, to the patient whose picture I have tried to draw, may be seen another man apparently suffering from quite a different affection (Fig. 26). He is propped up in bed. Instead of being thin and wasted, as the last patient, his face is puffy and heavy: his lips possibly are slightly cyanosed; and his arms, hands, trunk, legs, and feet are distended with oedema. It may be thought from the appearance of the oedema that it is a case of

acute nephritis, and an examination with this idea may be made of the scanty, dark-coloured urine. But this is found to be of high specific gravity, and to contain no albumin, or only a mere trace, so that the case cannot be one of acute Bright's disease. Careful observation will discover that the œdema is somewhat firmer than that of nephritis, and, in not a few instances, that it does not involve the scrotum. Occasionally cases are met with in which the œdema is peculiarly localised and fugitive. Attention is now directed to the heart, and here a bruit is discovered, besides other evidences of dilatation of the organ and of arterial relaxation, just as in the first case. The lungs are now examined, and there, too, one may or may not discover signs of single or double hydrothorax, although, probably, not to a very great extent. The lungs are themselves healthy. On getting him out of bed it is found that the patient can hardly walk, partly from breathlessness, partly on account of mechanical interference by the dropsy with the movements of the legs, partly, perhaps, from some degree of paresis. He has ankle-drop possibly;

Fig. 30. Berthon, Bentley.

and, if firm pressure be brought to bear on the calf muscles through the œdema, signs of hyperæsthesia of the muscles may or may not be elicited Knee-jerk is probably absent, and there is numbness of the shins and finger-tips. The tongue is clean, the appetite fair, and there is no fever. But there may be complaint of præcordial distress and even pain ; this is aggravated by a full meal, so that the patient is obliged to eat sparingly. The amount of urine is generally very much reduced to a few ounces even In this patient, therefore, there are the same signs of peripheral neuritis and of dilatation of the heart as in the other case. In addition, there is a somewhat firm œdema, which is not altogether cardiac; but, as its character and the circumstances in which it is found suggest, is probably connected partly with lesion of the nerves regulating urinary excretion, and partly with the play of transudation and absorption in the nutrition of the connective tissue.

Mixed paraplegic and dropsical cases.— In the next bed to this patient there lies, perhaps, another case which looks like a mixture of the two preceding There is œdema to some extent, particularly of the shins and feet, about the flanks and, very generally, over the sternum and root of the neck. There is numbness of the shins, there is some ataxia, there is muscular weakness and hyperæsthesia—particularly of leg and thigh muscles, there is absence of knee-jerks, there is cardiac bruit, and there are signs of dilatation of the heart and relaxed arterial tension. Just as in the other cases, the general health of the patient is unaffected, the tongue is clean, the urine though scanty is otherwise normal, and there is no fever.

Great variety in degree and combination of symptoms. All through the wards of the hospital dozens of similar cases may be encountered. Some are so trifling that they are up and moving about with more or less freedom ; others are so severely smitten that they lie like logs in their beds, unable

to move a limb or perhaps even a finger. Some are atrophied to skeletons; others are swollen out with dropsy; and some show just sufficient dropsy to conceal the atrophy the muscles have undergone. In some it will be noticed that the laryngeal muscles are affected, the patient being unable to speak above a whisper or to produce an explosive cough. In one or two the abdominal and the perineal muscles may be so profoundly paralysed that, when cough is attempted, at most a husky expiration is produced, whilst the belly is bulged forwards and the perineum shot downwards by the sudden contraction of the muscles of expiration.

Erroneous diagnoses. The novice in tropical medicine will be greatly puzzled for a time over these cases. I have seen them diagnosed as many kinds of diseases, and, until I had a little experience, have so diagnosed them myself. I have seen them called cardiac disease, locomotor ataxia, muscular rheumatism, progressive muscular atrophy, ascending spinal paralysis, and have over and over again seen them relegated to that refuge for ignorance—malaria, and called "malarial rheumatism," or "malarial paralysis," or, more pedantically, "malarial paraplegia," or "malarial neuritis."*

If the visitor has the curiosity to examine the blood of these patients, possibly in a proportion of them he will find filaria nocturna, or some of the other bloodworms; very likely he will then think that the cases are forms of filariasis, and he may construct theories to explain how the filaria produces the symptoms. Or, if he examines the fæces,

* Dr. Strachan has described (*Practitioner*, 1897, p. 477) a form of multiple peripheral neuritis which he calls "malarial." The disease is endemic, and very common in Jamaica. It differs from beriberi inasmuch as it is not attended with œdema, is frequently complicated with implication of the cranial nerves, and is rarely fatal. We have no accounts of any similar disease from other tropical countries. Probably, therefore, Dr. Strachan's neuritis is not malarial, but depends on some cause peculiar, so far as known, to Jamaica. The subject requires further study.

very probably in over 50 per cent. of the cases, or in some countries in nearly all the cases, he will find the ova of ankylostomum duodenale and, probably, those of trichocephalus dispar also. On this evidence he may conclude that these are cases of ankylostomiasis. He had better, however, not commit himself to such a diagnosis until he has ascertained how it fares with the rest of the population as regards these parasites, for he will find that the filaria, the ankylostomum, and the trichocephalus are quite as prevalent outside as inside the hospital, and in the healthy as well as in the sick.

Past history of patients.—On inquiry he will learn that most of the cases come from two or three centres where similar disease is endemic—from some particular plantation, mine, or village. He will also remark that the same places supply both atrophic-paralytic cases, and dropsical-paralytic cases; and he will also learn that many of the atrophic cases commenced with dropsical symptoms. From this he will make the important deduction that he is dealing, not with two diseases, but with two phases of the same disease; that sometimes this disease assumes atrophic features, sometimes dropsical features, and that sometimes it is of a mixed character. Many of the patients will give a history of fever at the outset of their troubles; in some there is a history of diarrhœa; in some the paralytic or dropsical symptoms developed very slowly; in others, again, they came on rapidly. In some there is a history of a similar attack the previous year, or a yearly attack for three or four years in succession. Some will tell that they have been ill for several months, others that they have been ill for a week or two only.

Its uncertain course.—He will learn that this disease, which is beriberi, commences slowly or suddenly; that it may be preceded by a period of intermitting languor, aching legs, slowly advancing œdema of legs or face; or that the patient may wake up some morning and find that during the night he

has become dropsical or paretic. Thus the disease may develop slowly or rapidly. Equally uncertain is its progress and danger; within a day or a week, or at any time during its course, it may assume fulminating, malignant characters. It may completely subside in a few days, or it may drag on for months. It may get well apparently and then relapse. It may, and generally does, clear up completely; or it may leave a dilated heart, or atrophied limb muscles with corresponding deformity. The variety in the severity, progress, and duration of beriberi is infinite; but in all cases the essential symptoms are the same greater or less œdema, especially over the shins; muscular feebleness and hyperæsthesia, especially of the legs; numbness, especially over the front of the shins, liability to palpitation from cardiac dilatation, and to sudden death from the same cause.

Progress of the cases. As the visitor watches the progress of the cases he will be astonished that those whom he thought examples of locomotor ataxia, or of progressive muscular atrophy, or of ascending spinal paralysis, gradually improve, begin to walk about, and finally quit the hospital quite well. He will be astonished to see, after perhaps a diffuse diuresis, the bloated carcass, that could hardly turn itself in bed, rapidly shrivel to nothing but skin and bone, and assume all the appearances of the atrophic cases; and, later, perhaps after many months, become rehabilitated, and, in due course, also walk out of the hospital quite well. He will notice that the cardiac bruits come and go; that the degree of dilatation of the heart is subject to fluctuations; that what seemed organic disease completely disappears

Cardiac attacks. But he will also be astonished, as he goes his rounds, to see so often empty beds where the day before lay men whom he considered by no means seriously ill—certainly not dying. Some day he will come on a patient whom the previous day he thought to be by no means seriously ill, actually *in extremis*. The poor fellow is propped up

in bed, he is struggling for breath, his face is purple, his eyes are starting out of his head, his whole attitude is expressive of the utmost distress; he has a horrible, tearing, boring, crushing pain under his sternum and in the epigastrium; the vessels of his neck are throbbing violently, his pulse is quick, small, intermittent, and his extremities are cold. In a short time the patient is dead. Some of the fatal cases, he will note, die quite suddenly as if from syncope; but most die in the distressing way described, evidently from paresis and over-distension of the right heart, complicated and aggravated by œdema of the lungs, or by diaphragmatic paralysis, by hydrothorax, or by hydropericardium.

Nomenclature and classification in beriberi.—For purposes of description, the paralytic atrophic cases are designated "dry beriberi" or beriberia atrophica; the dropsical cases, "wet beriberi" or beriberia hydrops; and those in which there is a combination of both conditions, "mixed beriberi." Sometimes the cases are classified according to the rapidity of development and gravity of symptoms into acute, subacute, and chronic. None of these classifications is good, seeing that they all refer to the same disease, and that one form may suddenly or more slowly merge into the other.

Ætiology.—*Sex, age, occupation, etc.*—Beriberi attacks both sexes. It occurs at all ages except early childhood and extreme old age, its favourite age being from about fifteen to thirty. It affects rich as well as poor. It is confined to no particular trade or occupation; if anything, it has a predilection for those who lead a sedentary life and are much indoors, as students, prisoners, and the inmates of asylums; it is apt to attack pregnant or parturient females. It is quite as common in the strong and full-blooded as in the weak and anæmic

Climatic conditions.—In countries in which there is a hot and cold season the epidemic outbreaks occur during the former, old cases improving and new

cases ceasing to crop up during the winter. In countries which are hot all the year round beriberi may appear at any time; most frequently, however, in such climates it appears during the rains.

Beriberi a place disease like malaria.—Everything points to beriberi being a disease of locality, in this respect resembling malaria. It further resembles malaria in being fostered by damp, by high temperature, and by its most often attacking those who sleep on or near the ground. As with malaria, though its explosion in any given individual residing in the endemic area may be solicited by fatigue, chill, privation, and other causes of physiological depression, it is not actually caused by such circumstances.

Influence of overcrowding.—Overcrowding seems to favour the outbreak of beriberi. This has, perhaps, a good deal to do with its frequency and virulence in such conglomerations of humanity as are found in Oriental jails, schools, mining camps, plantation lines, armies, ships. Unlike malaria, it is common enough in the middle of large cities as well as in villages and jungle land

Ship beriberi.—Unlike malaria, it is common in the native crews; more rarely, though occasionally, among the European officers and sailors of ships on the high seas and far away from any telluric influence The crowding in the damp forecastle and the exposure incident to a sailor's life seem to be among, though not the only, reasons for ship beriberi. Thus this form of the disease is often seen at the Seamen's Hospitals at the Albert Docks and Greenwich among the lascars and sidi-boys of steamers trading to India, the disease appearing perhaps months after the ships had left the East, sometimes even months after they had been lying in the London docks. Some years ago a number of these cases were admitted to the Seamen's Hospital at the Albert dock I had the curiosity to visit one of the ships from which several of the patients had been brought. I went into the forecastle. Although the weather was mild for Englishmen, it was evidently

very cold for the half-clothed lascars. They had a fire blazing in their quarters, every door, scuttle, window, and ventilator of which they had carefully closed. The place was suffocatingly hot, damp, and redolent of steaming humanity, and not very clean humanity either. I do not know how many men had stowed themselves away with their dirty rags in this place, but there was a crowd of them. Several had symptoms of beriberi, and were in their bunks. After seeing the forecastle I was taken to a little dark cell, an oblong den with a couple of bunks one on top of the other, located somewhere in the neighbourhood of the keel. There was no light, no means of ventilation, and barely standing room. There I found three men sitting on the lowermost bunk, all of them suffering from severe beriberi. One of them, I afterwards heard, died before morning; the others were sent to the hospital just in time to save their lives. The fact is that these epidemics of ship beriberi are fostered by the artificial conditions the ignorant lascars are allowed to bring about. They feel the cold of the English climate so much that, on entering British seas, they try to keep their quarters warm by lighting fires and stopping up all ventilators. By these means they create a hot, steamy atmosphere and a sodden state of the place they live and sleep in, which is a very good imitation of the tropical conditions the germ of beriberi requires for its development. In other words, these lascar sailors create an incubator on a large scale, which, should it chance to contain a beriberi germ, quickly becomes extensively infected and lethal.

Asylum beriberi.—Not very long ago exactly similar conditions, and with similar results, were produced by similar means in the Dublin lunatic asylum already alluded to. This asylum, built for 1,000 inmates, had 1,500 crowded into it. Any one, who knows what the atmosphere of even a well-regulated and not overcrowded dormitory in a lunatic asylum is like, can imagine what it becomes

in warm weather, where three patients are lodged in a place barely sufficient for two. The heat, the breath vapour condensed and streaming down the walls, the effluvia from the patients, the closed doors, the barred windows, the want of air, and the damp conspire to foster any germ of beriberi which evil chance may introduce into this incubator. These are just the conditions found in the tropics, and when these conditions are reproduced elsewhere, even in temperate climates, on the beriberi germ being accidentally supplied from without the result will be just the same.

Beriberi a germ disease, but probably not communicable from man to man. –Beriberi is undoubtedly a germ disease, for, as not a few facts have shown, the cause can be transported from place to place and, on encountering suitable conditions, will multiply as only a living organism can. I do not think, however, that the germ lives as a parasite in the human body, or that it exercises its pathogenic powers in a direct way, or that it passes directly from one human being to another like the germ of the ordinary infectious or directly communicable diseases. Nurses and medical men in hospitals where, perhaps, there may be hundreds of beriberi patients, do not catch the disease, nor in hospitals located outside the endemic districts does it spread to other patients. Of course, if hospitals are themselves infective, are themselves beriberi centres, beriberi may in that case attack patients admitted for other diseases, particularly, I think I have observed, for surgical disease—operation cases, in these circumstances it may attack nurses and medical attendants. Beriberi seems to resemble yellow fever in some of these respects.

Possibly caused by a toxin generated by a germ living in the patient's surroundings. –It is often remarked that when patients are removed from the endemic spots they at once begin to improve, and may be out of danger in a few days; whilst those who remain in the endemic area most probably go

from bad to worse, and very likely die. It is as if the place were infected by the germ, and not the individual; else, why should patients begin to mend so rapidly after they leave the locality? It is as if some toxin were generated in the soil or surroundings, and, rising up, were absorbed constantly and day by day; but when the spot in which the toxin is generated is quitted, and there is no longer a constant renewal of the poisoning going on, the effects, after a day or two, steadily and gradually wear out. This is not what happens where a germ is itself actually parasitic in the human body and the direct cause of disease; in such, disease and germ do not die out thus rapidly.

Pekelharing and Winkler's views.—Pekelharing and Winkler say that the beriberi germ is really introduced into the body, but as it can live there for a short time only, if beriberi disease is to be produced, fresh doses of the germ have to be constantly reintroduced. They have gone the length of saying that they have found the germ in question, a bacterium, in the blood, and that they have succeeded in cultivating it, and in inducing in the lower animals, by repeated injections of their cultures, symptoms like those of beriberi. There are various sources of fallacy about Pekelharing and Winkler's experiments, and their conclusions have not been accepted as yet by many good authorities.

Other germs. Besides the bacilli and cocci of Pekelharing and Winkler, many other germs have been described as the cause of beriberi, but on evidence altogether insufficient. The latest I have heard of is one fathered by Glogner, who says that the germ is an amœba—something like the malarial parasite in appearance and habits, and, like this, living in the red blood corpuscles.

I have many times looked for bacteria and microscopic parasites in the blood of beriberies, hitherto without success.

Nitrogen starvation theory. A favourite theory

some time ago was to the effect that beriberi was due to nitrogen starvation—to deficiency of nitrogenous elements in the dietary. In former years, beriberi used annually to attack quite one-fourth of the *personnel* of the Japanese navy. Now it is almost unknown in that service. This striking change coincided, in point of time, with the introduction into the Imperial navy of an improved ration, in accordance with a suggestion from Takaki who entertained this view about the influence of deficient nitrogen in food. It was inferred from the success following the change that the improvement in the health of the sailors was attributable to the increased amount of nitrogen in the new dietary. But the improvement could have been no more than coincidence; or, at most, the influence of the increased supply of nitrogen could only have been subsidiary. There were other hygienic reforms introduced about the same time as the improved dietary; these, doubtless, had their favourable influence. If we examine all the circumstances, we shall find that the nitrogen starvation theory does not tally with the facts of the peculiar geographical distribution of beriberi, its peculiar local limitations, its affecting rich as well as poor, its appearing in some houses and not appearing in neighbouring houses, and many other facts. For example, during an epidemic of beriberi in Singapore jail the male side of the prison was decimated, whilst not a single inmate of the female side was attacked, although both classes of prisoners had the same food and drank the same water. The only hygienic difference ascertainable between the two sides of the jail was, that whereas the male side was damp the female side was dry.

Various erroneous theories as to the causation of beriberi.—At one time Indian writers seemed somehow to have lost hold of this disease. Probably this was owing to its disappearance from the army there. As a consequence, the nature, and even the clinical features, of the disease came to be misunderstood; so that in

several works on Indian diseases it is stated that beriberi is of the nature of an anæmia, in others that it is an expression of scorbutus, in others, again, that it is a form of ankylostomiasis. These views are absolutely erroneous, and have been amply refuted in Burma, in the Straits Settlements, in Japan, and in many other places. Hæmocytometric observations have shown that anæmia, if it should happen to be present in a case of beriberi, is in no relation, except an accidental one, to the disease; so with scorbutus—a disease only too common in the underfed Oriental, and therefore likely enough to concur with beriberi in a certain proportion of cases; and so with the ankylostomum duodenale and the trichocephalus dispar—intestinal parasites which are extensively distributed throughout warm countries, in beriberi districts and in non-beriberi districts alike. In fact, beriberi has been attributed to all sorts of causes—to damaged grain, damaged fish, to rain, to wind, to heat, to cold, to rheumatism, and to many other things, amongst others, of course, like every tropical pathological puzzle, to malaria.

The germ viewed as a saprophyte. My idea about the matter is, as I have said, that beriberi is a germ disease; that the germ resides in the soil, in the houses and surroundings of beriberi spots; that it there distils a poison which, on being absorbed by man, produces neuritis, much in the same way that alcohol does. The soil is the infected medium; the man residing on it is poisoned, not infected. In the case of alcoholic neuritis—so like beriberi—the germ of the disease is the yeast plant; the culture medium, the saccharine solution; the toxin, the alcohol. The alcohol germ may be swallowed with impunity; not so the toxin it generates. So with beriberi: its germ lives in the soil; it produces some kind of toxin there; and this toxin, being inhaled or swallowed by man, produces in him a specific neuritis; and, just as man can carry the yeast plant from one place to another, so may he carry the beriberi germ. So

far as I have been able to interpret them, this is the only hypothesis which fits in with all the facts of the case.

Morbid anatomy and pathology.—There is very little to be said about the *post-mortem* appearances in beriberi which is not covered by the accepted descriptions of the lesions of peripheral neuritis. Central changes have not been made out with certainty, but there is a degeneration of the peripheral nerves—more especially of the distal nerves, and there is secondary atrophic degeneration of muscle, including that of the heart, which may be the subject of an acute fatty degeneration like that of diphtheria. If there is anything peculiar about the *post-mortem* appearances in beriberi, it arises from the somewhat special implication of the central and peripheral organs of the circulation—namely, dilatation of the heart, especially of the right side, and great accumulation of blood in the right heart and in the veins. In addition there is a marked liability in many cases to serous effusion into the pericardium, pleuræ, peritoneum, and cellular tissue. This liability to serous effusion, and the tendency to cardiac dilatation, may be said to be more or less distinctive of the beriberic neuritis as compared with other forms of multiple neuritis. It doubtless depends especially on vaso-motor disturbances, although cardiac weakness and partial suppression of urine may be contributory elements in its production. Œdema of the lungs is also not uncommon and has, probably, a similar pathology to the connective tissue œdema. There is no nephritis.

Mode of death.—The most practically important point in the pathology of beriberi is that which relates to the modes of death. The paresis and the atrophy of the voluntary muscles, the œdema of the connective tissue, and the serous effusions are, as a rule, not very serious matters—at all events as affecting life. But it is very different when paresis and degeneration seriously implicate the heart and the muscles of

respiration. In nearly all beriberics there is heart trouble arising, doubtless, from implication of the pneumogastric nerve and the cardiac plexus. In some patients the degree of implication is slight, but in others it is sufficient so to weaken the heart that death is inevitable. We cannot be quite sure in what cases the pneumogastric implication is likely to be serious, or in what cases it is likely to be slight. Often the mildest cases of beriberi, as judged by the degree of voluntary muscle paresis, or by the amount of œdema, are in reality the most dangerous. There appears to be an element of chance determining the nerves which the poison picks out. Sometimes one may see a case which is completely paralysed so far as legs and arms are concerned, and perhaps wasted to a skeleton; and yet this same patient may never have a serious symptom referable to his heart, or in any way threatening life. On the other hand, one may see a patient with very little paresis, very little œdema, and yet in a short time the heart may become involved, and he will die in a few minutes or hours. I presume the dilatation of the heart, the usual cause of death in beriberi, is favoured or brought about by a concatenation of several conditions; by the degeneration of the muscle fibre following nerve destruction, by imperfect systole in consequence of an interrupted nerve supply, by obstruction to capillary circulation in consequence of vaso-motor paresis both in the pulmonary and in the general circulation Once commenced, the cardiac dilatation tends to increase of itself; for the more the organ dilates, the more difficult does it become for it to contract, the greater the incompetency of the valves, and the more the blood stagnates in and over-distends it. The organ enters on a vicious pathological circle. Finally it becomes so distended that, like an overstretched bladder, it loses the power to contract altogether. The blood then rapidly accumulates in the great veins, the right auricle and ventricle are distended almost to bursting, and death is inevitable. This result is often

contributed to by the co-existence of pleural effusion, hydropericardium, paresis of the diaphragm, over-distension of the stomach by food or gas, and, above all, by œdema of the lungs. It can readily be understood how the establishment of any additional obstruction of this description would still further tax the dilated, enfeebled heart, and determine the fatal issue.

When we come to make a *post-mortem* in these cases we may find a heart slightly hypertrophied and enormously dilated, the right cavities distended with blood, the lungs and liver full of dark blood, and all the great veins engorged.

Prognosis.—This tendency to dilatation of the heart is the dangerous element in beriberi; it should always be before our eyes, and dominate our plans of treatment. It is wonderful how rapidly it may come on, and how rapidly it may prove fatal. These sudden deaths, occurring sometimes from syncopè—from instantaneous failure, as well as from the somewhat slower process of increasing over-distension—are constantly sprung on one in this disease. An absolutely favourable prognosis, therefore, ought never to be ventured on in even the mildest-looking case of beriberi, or so long as the patient is in the endemic area, or so long as the disease appears to be active. That is a lesson which is often, and sometimes painfully, borne in on the practitioner in beriberi districts.

Evidences of grave heart implication, such as pulsating cervical vessels, equal spacing of the intervals audible on auscultation, enlargement of cardiac dulness—especially to the right, epigastric pulsation, a rapid feeble pulse, cold extremities, cyanosis, dyspnœa, are significant of danger. *Paralysis of the diaphragm, of the intercostal muscles, extensive serous effusions, very scanty urine* are also unfavourable signs.

Vomiting.—No one can say when or how soon fatal implication of the pneumogastric and other cardiac nerves may take place, but vomiting is always an ugly and threatening symptom in beriberi; it

probably indicates that the former important nerve is being attacked. The Japanese, who have much experience of beriberi, regard the occurrence of vomiting as of fatal import.

Prognosis is improved if the patient is early removed (that is before the heart muscle, or the cardiac or respiratory nerves, are gravely degenerated) from the place in which the disease was contracted, to a healthy, non beriberic, high-lying locality.

Mortality. The mortality in beriberi varies in different epidemics and in different localities. On the whole, it is greater in low than in high latitudes, in the dropsical than in the atrophic forms, in the acute than in the chronic. In some epidemics it is as high as 30 per cent. of those attacked; in others as low as 5 per cent.

Diagnosis. Usually the diagnosis of beriberi is not difficult. Multiple peripheral neuritis occurring as an epidemic, or in a place or ship on which the disease had occurred on some previous occasion, as a rule, may be set down as beriberi. Sporadic cases may be difficult to diagnose, more especially if there is a history of alcoholism. The presence, actual or past, of œdema especially of œdema over the shins—and palpitations and other evidences of cardiac implication, are significant of beriberi. It must be borne in mind that slighter degrees of beriberic poisoning, evidenced only by slight analgesia of the pretibial skin area, by slight œdema of the same region, by slight hyperæsthesia of the calf muscles, and, perhaps, by impairment or absence of knee jerk, may be all the symptoms present. True rheumatism is rare in the tropics. Among natives, especially if their language is not understood, complaints of what may seem to be but rheumatic pains in the legs should always be carefully investigated, the knee-jerks tested, and signs of hyperæsthesia of the calf muscles sought for. The significance of these signs, of what may be described as larval beriberi, is too frequently

overlooked until some sudden death, which, with earlier recognition of the disease, might have been avoided, puts the practitioner on his guard. All paretic affections, all cases of œdema, all cases of palpitation, and all cases of rheumatic-like pains occurring among the natives of warm climates, therefore, should suggest the possibility of their being beriberi, and also the necessity for a detailed examination with this possibility in view.

Treatment.—The first and most important thing to be attended to in the treatment of a case of beriberi is the removal of the patient from the building, camp, or ship in which the disease was contracted. His condition warranting transport, if possible the patient must be got out of the endemic district. To leave a patient suffering from beriberi in the spot where he contracted his disease, is to leave him to continue absorbing the toxin that caused it; it is like allowing the victim of alcoholic neuritis to go on drinking. It is hardly possible for him to get well in such circumstances; it is often—in bad epidemics nearly always—tantamount to condemning him to death.

He should be removed to some dry locality; and, if such is available, sleep well off the ground in a thoroughly ventilated, sunny room situated in an upper storey. He ought to clothe sufficiently and feed well, taking care that the food is not of a bulky character, and that it contains a sufficiency of nitrogenous elements. Rice is found to be a bad food for beriberics; it is too bulky. Wheat flour is better, so is oatmeal; beans of different kinds seem specially suitable for these cases, as they are cheap, and contain much nitrogenous matter in a small compass. Animal food must enter into the dietary in reasonable amount. Milk and eggs are beneficial. The worst cases, particularly if there is any sign of serious cardiac implication, should remain in bed; but the mild cases had better spend the greater part of the

day in the open air. If the disease break out on shipboard, the crew—healthy and sick alike—should be kept out of the forecastle, and, so far as possible, made to sleep on deck, properly protected from the weather by an awning. The seriously affected patients should take little fluid, and, with a view to diminish to some extent the bulk of blood in the vessels and heart, the bowels should be kept free by some saline aperient.

In cardiac cases small doses of digitalis or of strophanthus seem to do good. Should signs of acute cardiac distress appear, full doses—three, four, or five drops of the 1 per cent. solution of nitro-glycerine are indicated. This must be repeated every quarter or half hour, and kept up until the threatening symptoms pass away. In suddenly developed cardiac attacks inhalations of nitrite of amyl, pending the operation of the nitro-glycerine, may be given. It is well that these two drugs be in the hands of properly instructed ward attendants, so as to meet cardiac complication on its earliest appearance. There is often no time to send for the doctor. Should, in spite of these means, signs of cardiac distension and failure persist and increase, there must be no hesitation in bleeding the patient, taking eight to ten ounces from the arm if it will flow, or, this failing for any reason, from the external jugular. Often, as the blood flows, rapid amelioration of the alarming condition sets in, and the patient is, for the time being, tided over an acute danger and given another chance. The bleeding should be repeated if the alarming symptoms recur, as they are pretty sure to do. Oxygen inhalations, if available, are worth trying in cardiac attacks. Pleural and pericardial effusions should be sought for, and, if deemed to be interfering in the slightest degree with the circulation or respiration, drawn off with the aspirator.

Provided the patient has been removed from the spot where he was being poisoned, and provided

he can be tided over the first few days, he will probably recover; but in a serious case, should he remain in the place where his disease was acquired, though he may get over one or two cardiac attacks, the risk to life in bad epidemics is very great indeed, and he will almost surely die.

For the atrophy of the muscles and anæsthesia of the skin, faradisation and massage are of great service, and should be employed so soon as the muscular hyperæsthesia has subsided not before. Strychnine, arsenic, and nitrate of silver are in repute as tonics in these circumstances. Care should be taken that permanent deformity does not occur from contraction of muscles. Foot drop should be counteracted by Phelps's talipes splint with an elastic accumulator, and any other threatening deformity appropriately met. Relapses must not be risked by a return to the original source of infection A sea voyage has often a marvellously restorative effect.

When beriberi breaks out in a school, jail, or similar institution the place should be emptied of its inmates as soon as possible; at all events, those parts of the building in which the disease has appeared ought to be cleared out and not reoccupied until they have been thoroughly cleansed, disinfected, ventilated and dried. Overcrowding must be strictly avoided. Ventilation must be effective. The dietary should be revised and, if necessary, have rice eliminated from it as much as possible; in the place of rice, meat, flour, or beans should be substituted. All the inmates should be obliged to pass a considerable time of every day in the open air; their knee-jerks should be tested, and their legs examined for numbness, œdema, and muscular hyperæsthesia from time to time. Any suspicious case should be removed at once.

Should beriberi appear on board ship, besides the precautions already indicated, special means of disinfection must be employed Rotten planking and bilge water must be removed from the quarters of the crew; the sound woodwork should be scraped and

painted; disinfectants should be freely and frequently employed; clothes and sea-chests washed, and every means necessary to destroy lurking germs vigorously practised.

In beriberi countries low-lying, damp situations should be avoided as building sites. The sleeping quarters, especially, should be raised well off the ground, and located, if possible, in an upper storey; all rooms should be so arranged as to be easily flushed with fresh air and flooded with light.

CHAPTER XV

EPIDEMIC DROPSY.

Definition and description.—A specific, epidemic, communicable disease running its course in from three to six weeks, and characterised by the sudden appearance of anasarca, preceded in most instances by fever, vomiting, diarrhœa, or by irritation of the skin; and often accompanied by a rash, by fever of a mild, remitting type, by disorder of the bowels, and by pronounced anæmia. The case mortality varies from 2 to 40 per cent., death being sudden and depending upon œdema of the lungs, hydrothorax, hydropericardium, or other pulmonary and cardiac complications.

History and geographical distribution.—The foregoing is a concise description, drawn principally from McLeod's account (*Trans. Epidem. Soc. Lon. N.S.*, vol. xii.) of a disease which appeared in Calcutta, it is believed for the first time, in the cold weather of 1877-78, of 1878-79, and 1879-80. On each occasion it disappeared with the advent of the hot weather. The same disease broke out at Shillong, Assam, 5,000 feet above the level of the sea, in October, 1878; at Dacca in January, 1879; at south Sylhet, in the cold weather of 1878-79; and in Mauritius (Lovell and Davidson), having been imported from Calcutta, in November, 1878. There are no trustworthy accounts of its occurrence elsewhere, although certain vague statements seem to indicate that it appears at times in other parts of India. In Mauritius it prevailed until June, 1879, attacking about one-tenth part of the coolie population, of whom 729 died, a mortality of about 2 or 3

per cent. At Sylhet there were no deaths; at Shillong the mortality was also insignificant; but in Calcutta the death-rate in those attacked was estimated as high as 20 to 40 per cent. Coolies and natives were alone affected, Europeans enjoyed a complete immunity. In Calcutta the disease was confined to a particular quarter; here it attacked families and groups of people, slowly extending its area, but at no time becoming generally epidemic throughout the city. The disease has not recurred in Calcutta since 1880; at all events, if it has done so it has not been recognised.

Special symptoms.—*Dropsy* was almost invariably present. It usually appeared first in the legs, and in some instances was confined altogether to the lower extremities; in others it spread and involved the entire body. Occasionally it was very persistent, lasting and recurring even after the patient was well in other respects.

Fever was also a very constant symptom; sometimes it preceded, sometimes it accompanied, sometimes it succeeded the dropsy. It was rarely high, ranging usually from 99° to 102°; in a few cases possibly from malarial complications it reached 104°. Rigors were rare.

Diarrhœa and vomiting generally ushered in the disease in the Mauritius epidemic. In Calcutta these symptoms were not so frequent, although they were by no means rare there, occurring at both the earlier and later stages. Dysentery was common in the Calcutta epidemic.

Nervous symptoms—such as burning, pricking, itching, and feelings of distension of the skin, and sometimes limited to the soles and feet—often preceded the dropsy. Distressing aching of muscles, bones, and joints, worst at night, was usual. Anæsthesia of skin areas and paresis of muscles were never observed in Mauritius. Harvey remarked two cases in Calcutta exhibiting doubtful paretic symptoms; these are the only two recorded

in which there was anything resembling the paretic symptoms usually so prominent a feature in beriberi.

An exanthem, erythematous on the face, rubeolar on the trunk and limbs, was frequently seen in Mauritius, less frequently in Calcutta. It appeared about a week after the œdema, and lasted from ten to twelve days.

Circulation and respiration. - Disturbances of the heart and circulation were prominent features in nearly all the cases. The pulse was weak, often rapid and irregular; cardiac bruits were also noted. Breathlessness on exertion occurred in all cases, severe orthopnœa in many. Signs of pleural and pericardial effusion, of œdema of the lungs or pneumonia, and of cardiac dilatation were common in Calcutta.

Anæmia was usually present and marked; so were wasting and prostration. Scorbutic symptoms occasionally showed themselves.

The *liver, spleen and kidneys* were not specially affected. The urine was rarely albuminous.

Morbid anatomy. Beyond general œdema and occasional pleural and pericardial effusion, nothing special was remarked *post-mortem*.

Ætiology.—Both sexes were attacked; children under puberty were less liable than adults, sucklings were seldom affected. The weak and the robust were equally susceptible. There are no observations on the germ of the disease; there is distinct though indirect evidence, however, of its portability and of its communicability. But as to whether it is directly communicable from man to man, or whether it, or its product, is indirectly transmitted through some unknown medium, has not been determined. Evidence of its capacity for remaining latent for a considerable period is supplied by the history of the successive epidemics in Calcutta. The disease could not have been a very catching one, seeing that no medical man was attacked, and that, except in the case of Mauritius, it spread but slowly.

Identification. -McLeod, after a careful analysis

of all the available evidence, concludes that epidemic dropsy is a disease *sui generis*. At the time of its occurrence in Calcutta many of the physicians there looked upon it as a form of beriberi; and, indeed, in many respects it resembles very closely those cases of beriberi in which dropsy is a prominent symptom, and in which the nervous phenomena are slight or altogether absent. But in epidemics of beriberi such cases are the exception—in fact, are very rare, and always concur with others in which nerve symptoms are pronounced, and with purely atrophic cases; such were not seen in either the Calcutta or the Mauritius epidemics. In epidemic beriberi the mortality is much higher than it was in the Mauritius, the Shillong, or in the Sylhet epidemics. Furthermore, beriberi is a much more chronic disease, is not accompanied by an eruption, and but seldom with well-marked fever.

Treatment.—In the absence of anything like precise knowledge of the cause and pathology of epidemic dropsy, treatment must be entirely symptomatic. Mild purgatives, the exhibition of digitalis when there is evidence of cardiac weakness, and the occasional use of the nitrites in the fits of apnœa, might prove serviceable. During convalescence iron and arsenic are indicated.

CHAPTER XVI.

NEGRO LETHARGY, OR THE SLEEPING SICKNESS OF THE CONGO.

Definition.—A disease, so far as known, limited to tropical West Africa. It is characterised by a peculiar and slowly increasing lethargy, and by other morbid nervous phenomena. After a chronic course it probably invariably terminates in death.

Geographical distribution.—In West Africa, between Senegambia to the north, and the Portuguese territory to the south of the Congo, there occurs among the natives of certain districts a peculiar disease characterised by a gradually deepening lethargy and somnolence and other cerebral symptoms which culminate in death. Locally this disease is known as "the sleeping sickness."

Its distribution in the endemic area is peculiar. In some limited districts it is extremely prevalent, whilst in neighbouring districts it may be completely absent. Recent accounts from the Lower Congo tell us of its extreme frequency in that district; we have also some meagre accounts of its occurrence in the upper reaches of that river. Corre tells us that in some parts of Senegambia it is equally common. It is said to be unknown on the lower part of the Niger (Crosse), at the mouth of the Congo, at Sierra Leone, and at a good many other places in the general endemic area. Its visitations seem to come and go. After decimating a village it may quite disappear for a time, migrating temporarily, as it were, to some neighbouring village. Accurate information is wanting on this, as on many other matters relating to this interesting disease. This

much, however, is known—that it is an endemic which is liable to epidemic outbursts. So great is the terror of the natives, when the disease appears among them, that they may even abandon their villages. A peculiarity about sleeping sickness lies in the fact that, although it can be acquired in certain places only, the symptoms of the disease may appear for the first time in quite another country, and many years (up to seven the negroes say) after the endemic region has been quitted For example, a native of the endemic area may leave his country, make a voyage to England or to the West Indies, reside there apparently in good health for several years, and then, at the end of this term, exhibit for the first time the characteristic symptoms, and ultimately die of the disease. In the days of the slave trade sleeping sickness was frequently seen among the negroes in the West Indies; but it was never seen in negroes who were born in the West Indies and who had never visited Africa, being met with only in those who had come from, or had resided at one time in, the latter continent. Therefore although the symptoms may develop anywhere, the cause of the disease must be strictly endemic. Sleeping sickness is not exclusively confined to the negro race, but only to the negro country. It has been seen in mulattos and in Moors, possibly in Europeans. It is unknown as an endemic in the north, east and south of the African continent, being limited apparently, as already indicated, to the basins of the Senegal, the Niger, the Congo, and the minor intermediate rivers.

Symptoms. Sleeping sickness begins very insidiously. Those who are familiar with the disease are said to be able to recognise it in its earliest stages. The patient acquires a peculiar listless and morose manner, a somewhat melancholy expression of countenance, a certain fulness and puffiness about the face, a drooping of the upper eyelids; he or she is liable to headache, to attacks of vertigo, to evanescent

flashes of fever, sometimes to diarrhœa and other intestinal disturbances. By-and-by, after a variable period of weeks or months, he begins to experience feelings of excessive lassitude, and of disinclination or of inability for the daily task; generally, too, there is a desire and liability to fall asleep at unusual times. He may fall asleep while at work, while at his amusements, and even while he is eating. He is readily fatigued; when he does speak, he complains of his weakness. He appears to feel chilly, for he likes to lie about in the sun. The lethargy and somnolence get better and worse; on the whole, they tend slowly to become aggravated. By-and-by, the patient seeks to seclude himself; he ceases to take a part in conversation, although, when obliged to speak or to answer a question, he may do so intelligently enough. Gradually he becomes more silent, more taciturn, and he sleeps, or, rather, appears to sleep, almost constantly. If he is forced to walk or move about, he does so as if half awake or as if intoxicated, staggering about. His temperature may be sometimes elevated during the attacks of irregular fever; at other times, and generally, it is distinctly subnormal. Limited patches of cutaneous anæsthesia may sometimes be discovered. A certain amount of muscular tremor is now observed, and muscular power diminishes. He takes to bed or lies about in a corner of his hut, indifferent to everything going on around him, though still able to speak and to take food when it is brought to him. At this more advanced stage, however, he never spontaneously enters into conversation or even asks for food. As torpor deepens he forgets even to chew his food, falling asleep, perhaps, in the act of conveying it to his mouth, or with the half-masticated bolus still in his cheek. In other respects his health seems good. When he can be got to eat, the food is digested and properly assimilated. There is no wasting at first, and fæces and urine are regularly voided. As time goes on, however, he begins to lose flesh; muscular

tremor, in the hands and tongue especially, becomes very marked, and choreic movements may occur in one or more limbs. He may be seized with localised or more general convulsions, which are apt to be followed by paralysis of the convulsed part. Later, bed sores begin to form, and the lips swell and saliva dribbles from the mouth. Gradually lethargy deepens, nutrition fails, the body wastes, bed sores extend, and, finally, the patient may become comatose and so die; or he may sink from slowly advancing asthenia. Possibly he is suddenly attacked with general and fatal convulsions.

Such is the ordinary course of sleeping sickness; but its manifestations are subject to considerable variation. Occasionally it seems to be arrested in its progress; though, very generally, once established, it proceeds to the fatal issue without material alteration for the better. Mania, occasionally noisy or violent, sometimes occurs; this, and other psychical and physical symptoms like those in the general paralysis of the insane, are not unusual in the earlier stages.

There are one or two additional symptoms, not referable to the nervous system, which are frequently observed in sleeping sickness; one is enlargement of the cervical glands; another is a papulo-vesicular eruption, especially pronounced in the chest, and attended with intense pruritus. The skin as a whole becomes dry, lustreless, and scurfy, and the hair is said to acquire a reddish tinge.

In those instances in which the points have been investigated the fundus oculi has been found normal, the superficial reflexes active, the deep reflexes somewhat exaggerated.

The duration of sleeping sickness is very variable; it may be anything from four months to as many years, a good deal depending on the way in which the patient is tended.

Pathological anatomy.—Manifestly, sleeping sickness is a brain disease, although hitherto no

morbid appearances in connection with the nervous system, or with any organ, sufficient to account for the symptoms, have been discovered.

Ætiology.—Sleeping sickness affects either sex and any age, and appears to be in no way influenced by occupation, temperament, food, or heredity. It has been attributed, on altogether insufficient grounds, to many things; but the true cause has not been definitely ascertained.

Remarking the singular correspondence which seems to obtain in the distribution of this disease and that of filaria perstans, and the well-ascertained facts that the disease may declare itself, and that this parasite can remain alive, years after the endemic area has been quitted, I have suggested that filaria perstans may in some way be responsible for sleeping sickness. If this be really so, it is hard to say in what way the parasite operates. It is just possible, however, that by interfering with the nutrition of the brain, as by blocking the vessels, or by destroying some organ, such as the pituitary gland, necessary for the nutrition of the brain, the parasite, in unknown and peculiar circumstances, may bring about this singular disease. As a matter of fact, I have found filaria perstans in several cases of sleeping sickness, and the parasite is now known to be exceedingly prevalent in a large proportion of the inhabitants of the endemic districts. The subject requires further investigation.

Diagnosis.—Sleeping sickness has been confounded with beriberi; but if it be borne in mind that the former is a disease of the central nervous system, whereas the latter is a disease of the peripheral nerves, such a mistake is not likely to occur.

Treatment.—Purging appears to do good temporarily. Arsenic in very large doses has also seemed to be followed by improvement, and even by arrest. Lately, I have heard from Dr. Sims, of Stanley Falls, that hypodermic injection of testicular fluid has cured several cases. On the supposition that disease of the

pituitary gland is responsible for the symptoms—which in many respects are like those resulting from pituitary gland disease—it might be worth while to try the administration of this body in some form, on the same principle as thyroidin is given in myxœdema.

If filaria perstans be at the root of the disease, care in the matter of drinking-water is indicated as a prophylactic measure.

SECTION III.—ABDOMINAL DISEASES.

CHAPTER XVII.

CHOLERA.

Definition.—An acute, infectious, epidemic disease characterised by profuse purging and vomiting of a colourless serous material, muscular cramps, suppression of urine, algidity and collapse, the presence of a special bacterium in the intestine and intestinal discharges, and a high mortality.

History and geographical distribution.—It is probable that from remotest antiquity cholera has been endemic in Lower Bengal,* and that thence, from time to time, it has spread as an epidemic over the rest of India. European physicians observed it there in the sixteenth, seventeenth, and eighteenth centuries, but it was not until the great epidemic extension of 1817 that the disease seriously attracted the attention of the profession in Europe. In that year cholera began to spread all over Asia, extending eastwards as far as Pekin and Japan, southwards to Mauritius, and westwards to Syria and the eastern shores of the Caspian. Stopping short at Astrakhan in 1825, it did not on that occasion invade Europe.

European epidemics.—In 1830 cholera visited Europe for the first time. Advancing through Afghanistan and Persia, it entered by way of Russia,

* Though it is customary to speak of Lower Bengal as the home of cholera, it is by no means certain that other eastern localities have not some claim to a similar distinction—Bankok, Canton, and Shanghai, for example. Dr. Henderson, in his health reports, indicates that the disease is rarely absent during the summer months from the latter city; the same may be said of Bankok and of Canton.

and swept as an epidemic over nearly the entire continent, reaching Britain at the beginning of 1832. During the same summer it crossed the Atlantic to Canada and the United States. This epidemic did not die out in Europe till 1839.

Since that time there have been at least five European epidemics — 1848-51, 1851-55, 1865-74, 1884-86 and 1892-95. Great Britain has been seriously involved in four only of these epidemics— namely, in 1832, 1848, 1854-55, and in 1866. On the occasion of the last two European epidemics, although frequently imported, the disease did not spread in Britain. America has not been so fortunate; for, although the 1870-73 epidemic practically spared Great Britain, it crossed the Atlantic and, entering by way of Jamaica and New Orleans, raged for a time in the United States.

From a study of the march of these various epidemics, it is to be concluded that cholera reaches Europe by three distinct routes:—*First*, viâ Afghanistan, Persia, the Caspian Sea, and the Volga valley; *second*, viâ the Persian Gulf, Syria, Asia Minor, Turkey in Europe, and the Mediterranean; and, *third*, viâ the Red Sea, Egypt, and the Mediterranean.

With certain exceptions, hereafter to be mentioned, there is hardly an important country in the world which has not, at one time or another, been visited by cholera in the course of some of its pandemic extensions.

Ætiology.—*The disease is carried by man.*— The study of the various epidemics shows that in its spread cholera follows the great routes of human intercourse, and that it is conveyed chiefly by man, probably, in its principal extensions, by man alone, from place to place. In Britain and the United States, for example, the places first attacked have been invariably seaports in direct and active communication with other ports already infected. In India, although the problem is much more difficult

to unravel, the influence of human intercourse in diffusing the disease in certain instances can be distinctly traced. Thus the extensive pilgrimages, so frequent in that country, are a fruitful source of its rapid spread. During these gatherings hundreds of thousands of human beings are collected together in highly insanitary conditions—as at the Hurdwar and Mecca pilgrimages. Cholera breaks out among the devotees, who, when they separate, carry the disease along with them as they proceed towards their homes, infecting the people of the places they pass through. Cholera never travels faster than a man can travel; but in modern times, owing to the increased speed of locomotion and the increased amount of travel, epidemics advance more rapidly and pursue a more erratic course than they did sixty years ago.

Isolation secures immunity. — In the case of isolated countries the absence of active and frequent intercourse with the outer world favours immunity, even during approximately pandemic extensions. Thus, though so near to the home of cholera, the Andaman Islands have never been visited by the disease. Similarly, Australia and New Zealand hitherto have enjoyed practical exemption. The same can be advanced of the Pacific islands, the Cape of Good Hope, the west coast of Africa, Orkney and Shetland, Iceland, the Faroe Islands, and many of the islands of the Atlantic.

Its unequal diffusion in the endemic and epidemic areas.—Although cholera is always present in some part of the endemic area in Bengal, it is not equally diffused there, nor is it equally common at all seasons and every year. Thus, even within this area, there are places which enjoy an absolute or a relative immunity, and there are seasons and years of special prevalence. It has also to be remarked that the season of immunity for one place may be the season for prevalence in another place, and *vice versâ*. The same observations apply to the areas of epidemic extension.

When cholera extends as an epidemic, its course

is often singularly erratic. Some places, apparently in the direct line of advance, are passed over, to be attacked perhaps at a later period. Similarly, certain districts of a town may be spared, while other parts of the same town are ravaged by the disease.

Local conditions favouring its presence.—On the whole, it may be said that low-lying districts, particularly those along the banks of rivers, are more subject to the disease than high and dry situations; and that overcrowding and unhygienic conditions generally conduce to its prevalence. The principal and special element, however, which determines the diffusion of cholera is, undoubtedly, the character of the water supply.

Cholera in the main a water-borne disease, entering by the stomach. From time to time many theories of the cause and nature of cholera have been put forward, many of them very absurd and manifestly incorrect. Most of these have now been definitely abandoned in favour of the theory that the cause of cholera is a specific germ which, in the main, is water-borne. The evidence in favour of this view may be regarded as being almost conclusive, although there is still some room for doubting whether the germ itself has really been discovered.

The earliest, and still one of the most telling pieces of evidence in favour of the water-borne theory of the diffusion of cholera, we owe to the late Dr. Snow. In August, 1854, cholera was epidemic in parts of London, notably in the neighbourhood of St. Anne's, Golden Square. A child at 40, Broad Street, after an illness of three or four days, died of the disease on the 2nd of September. The discharges had been thrown into a leaky cesspool which, as was subsequently discovered, drained into a well only three feet away. This well supplied the neighbourhood with drinking water. On the night of the 31st of August cholera broke out among those who used the water of this particular well, very few escaping an attack. On the 2nd of September a lady died

of cholera in Hampstead. Attention was specially called to this lady's case, as hitherto the disease had not been seen in that district. On inquiry it was found that this lady had been habitually supplied with drinking water from the Broad Street well referred to. She had formerly resided in Broad Street and had retained a liking for the water from this particular well. She drank some of the water which had been procured on the 31st of August, both on that day and again on the 1st of September. On the latter day she was seized with cholera. A niece, on a visit to this lady, also drank some of the same water; she, too, was attacked by cholera and died. A servant also drank the water; although she suffered to some extent, she recovered. So far as could be ascertained by careful inquiry, these people had had no connection whatever with the cholera districts except through the water fetched from this particular Broad Street well. Cholera, as mentioned, was not epidemic at Hampstead at the time. The inference that the germ had been conveyed in the polluted water is difficult to avoid.

Another remarkable illustration of the diffusion of the cholera germ by water is supplied by the recent epidemic in Hamburg. At the time, the hygienic conditions under which the inhabitants of the contiguous cities of Hamburg, Altona, and Wandsbeck lived were practically identical, save in the matter of water supply. Hamburg and Altona both drew their water from the Elbe; but, whereas the water distributed to the people of Altona was most carefully filtered, that supplied to the people of Hamburg was simply pumped up from the river and passed directly into the mains without filtration or purification of any description. The Wandsbeck water came from a lake and was filtered. In Hamburg, during the epidemic, there were 8,605 deaths from cholera, equal to 13·4 per thousand; whereas in Altona only 328 deaths occurred, equal to 2·1 per thousand. The death rate in Wandsbeck was similar to that of Altona.

Hamburg and Altona are contiguous and practically one city. At one part a street forms the boundary between the municipalities. On one side of this street, the Hamburg side, there were numerous cases of cholera; on the Altona side there were no cases. The houses on both sides of the street were of the same character, and occupied by the same class of people. The only difference, so far as could be ascertained, was in the water supply: the houses on the healthy side of the street received Altona water; those on the cholera-stricken side, Hamburg water. It was remarked that a certain group of houses on the Hamburg side remained free from the disease. On investigation it was found that, unlike the other houses on the same side, these houses derived their water supply from an Altona main.

As regards its relation to the water supply this Hamburg epidemic is the exact counterpart of what happened in South London in 1854. Formerly this district was supplied with water by two companies—the Southwark and Vauxhall Company and the Lambeth Company. Both companies drew their water from the Thames—the latter from near Hungerford Bridge, the former from near Battersea Fields. The epidemic of cholera which visited London in 1849 was especially severe in South London. Subsequently, the Lambeth Company removed its intake higher up the river, to Thames Ditton, and consequently the water it supplied at the time of the 1854 epidemic had improved in quality. The Southwark and Vauxhall Company did not change their intake, and in 1854 they were still drawing their supply from the river near Battersea Fields. When cholera visited London in that year the death-rate from the disease in the houses supplied by the Southwark and Vauxhall Company amounted to 153 per 10,000 inhabitants; whereas that in houses supplied by the Lambeth Company was only 26 per 10,000. The mains of the two companies ran side by side, some houses receiving the water of one company, some that of the other.

During the Hamburg epidemic it was also found that the incidence of cholera was three times greater among those who used the town water than among those who got their supplies from wells. These, and many similar facts which might be adduced, clearly point to water as a principal medium for the diffusion of the cholera germ.

The virus contained in the dejecta. — Evidence, equally conclusive, tends to show that the germ on being swallowed by man multiplies in his alimentary canal, and, on being voided in the dejecta, subsequently finds its way by a route more or less direct to water again in which, under favourable conditions, it continues still further to multiply. An illustration, amounting almost to proof, of the fact that the germ of cholera is contained in the stools of cholera patients is supplied by Macnamara. Some of the characteristic rice-water discharge from a cholera patient got mixed accidentally with a few gallons of water. This was exposed to the sun for twelve hours. Early the following morning nineteen persons each drank about an ounce of the mixture. Within thirty-six hours, five of these nineteen persons were seized with cholera.

Conditions of infection are complex.—It is evident that the ingestion of the germ is a necessary condition for the production of the disease, but there are many facts which render it equally evident that this is not the only condition. Were it the only condition, then every one of those individuals referred to by Macnamara would have sickened. What the other necessary conditions may be it is hard—in the present state of knowledge, impossible—to say.

There is reason to believe that not only are these conditions complicated as regards the susceptibility of the individual, but also that they are equally complex as regards the germ itself in relation to its pathogenetic, proliferating, and diffusing properties.

The germ of cholera.—*Early views.* Since European pathologists first directed their attention

to the subject, many views have been entertained as to the exact nature of the cause of cholera. Some of these views were of the most fantastic description. Mysterious atmospheric and telluric conditions were invoked, and superstitious notions worthy of the Middle Ages, only a very few years ago were freely ventilated even in high places and by educated minds. Among those who ventured to formulate definite and more reasonable hypotheses some considered that cholera, like the more familiar exathematous fevers, was directly contagious. Others thought that it was not directly contagious, but that it was communicated by the evacuations of the sick after these evacuations had undergone some peculiar fermentative process outside the human body. Others, again, as Von Pettenkofer, regarded the virus as a chemical ferment which developed in the soil under certain unknown epidemic conditions.

Discovery of the comma bacillus.—Since the rise of the germ theory of infective disease most of these speculations have been definitely abandoned; or they have received more precise expression in the view that cholera is caused by a certain bacterium, known as the comma bacillus or cholera vibrio, which Koch discovered to be practically invariably present in the stools and intestinal contents of cholera patients. This bacterium Koch first discovered in Egypt in 1883. Believing in its importance, he afterwards proceeded to India on a special mission, and there, in Calcutta, in 1884, he found the same bacterium in the intestinal contents of forty-two fatal cases, and in the stools of thirty other cholera patients, in fact, he found it in every case of the disease examined. Moreover, he entirely failed to find it in any other disease or in healthy discharges. These observations, so far as they concern the presence of the comma bacillus in cholera stools, have been abundantly confirmed by many other workers; so that the presence or absence of this bacterium is now regarded as a trustworthy and valuable practical test of the choleraic or

non-choleraic nature of any given case of intestinal flux; and this even by the opponents of Koch's special view as to the nature of the relationship of the bacterium in question to the disease with which it is so intimately associated. If only on account of its diagnostic value the comma bacillus, therefore, is an organism of importance; but as many high authorities regard it as a necessary concomitant and even as the actual germ and true cause of Asiatic cholera, the vibrio acquires an importance of the first rank.

The comma bacillus; description.—The comma bacillus (Fig. 27) is a very minute organism, 1·5 to

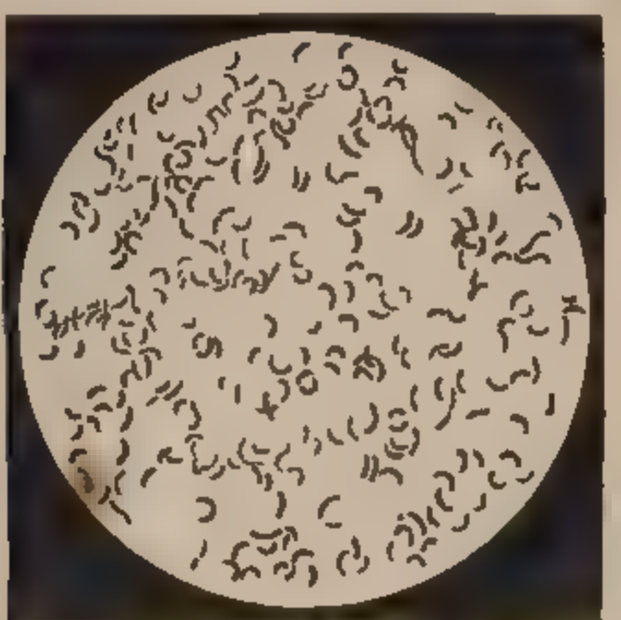

Fig. 27.—Cholera bacillus. Agar cult[illegible] stained with. × 1000. (*Muir and Ritchie.*)

2 micromillimètres in length by ·5 to ·6 micromillimètres in diameter—about half the length and twice the thickness of the tubercle bacillus. It is generally slightly curved, like a comma; hence its name. After appropriate staining at each end, or at one end only, flagella can be distinguished; sometimes one, sometimes, though less frequently, two. These flagella are of considerable length—from one to five times that

of the body of the bacterium; their extreme tenuity renders them difficult to see in ordinary preparations. The flagella are not always present during the entire life of the parasite. In virtue of this appendage, the bacillus exhibits very active spirillum-like movements. The individual bacilli, when stained, show darker parts at the ends or at the centre, suggesting the possibility of spore formation; this point has not been definitely settled, however. Sometimes in cultivations two or more bacilli are united, in which case an S shaped body is the result; or it may happen that several bacilli are thus united together, producing a spirillar appearance.

The comma bacillus is easily stained by watery solution of fuchsin, or by Loffler's method, dried cover-glass films being used. Dilute solution of methyl violet mixed with the intestinal contents and placed on a slide suffices for partial staining.

The bacillus grows best in alkaline media, at a temperature of from 30° to 40° Cent. Growth is arrested below 15°, or above 42° Cent., a temperature over 50° Cent. kills the bacillus. Meat-broth, milk, blood serum, nutrient gelatine, or potato, are all suitable culture media. Nutrient gelatine and potato are the most convenient for diagnostic purposes.

In gelatine plate-cultivations minute white points appear, around these the gelatine liquefies, and the colony of bacilli sink into a funnel or bubble-shaped depression. By the end of the second or third day, the cultivation is besprinkled with such depressions, liquefaction spreading peripherally until it involves the entire surface of the gelatine. The colonies are white or yellowish, very irregular in shape, granular, and shining like so many particles of ground glass. Later they assume a peculiar roseate hue, said to be absolutely characteristic.

In gelatine stab cultures the growth at first is most active near the surface, but later, the colony sinking, liquefaction advances most below the surface of the gelatine, so that a bubble-shaped appearance is

then produced. Later still, as growth proceeds along the needle track, a finger-shaped liquefaction results, which in time extends to the sides of the tube. At the bottom of the liquefied area there is an accumulation of a white mass of bacteria; at the top a scum of bacteria in various stages of degeneration is formed. These cultures may die after five or six weeks.

Agar is not liquefied, and in it the cultivations retain their vitality longer. On potato, at 20° to 30° Cent., the culture appears as a thin, brownish, porcelain-like film. In broth, some of the bacilli form a scum on the surface; others, falling in masses to the bottom, leave the body of the liquid clear.

Although, taken together and in conjunction with the morphological appearances, these culture characters are fairly distinctive, nevertheless certain other bacteria, such as Finkler's spirillum, behave very similarly; and, as the microscopic features of these other bacteria in some instances are very much like those of the cholera vibrio, a mistake is easily made. The production of what is known as "cholera red" by the addition of pure sulphuric acid (indol reaction) to a culture in peptonised broth, is also not quite distinctive of the cholera vibrio, for a similar reaction is produced by some other bacilli.

In careful and practised hands, however, the diagnosis of cholera by the microscopic and cultural characters of the vibrio may be made with practical certainty.

Is the comma bacillus the germ of cholera?—Although it may be safely asserted that cholera is intimately associated with the comma bacillus, it does not necessarily follow that this organism is the cause of cholera. Many attempts have been, and are being, made to establish such a relationship. Nevertheless, what may be considered as absolute proof is still wanting; such proofs as alone can be afforded by the production in man, or in the lower animals, of a disease in every respect like cholera by the administration of pure cultures of the comma

Variability of the cholera microbe. Bacteriological studies, always difficult, are extremely so in the case of the cholera microbe owing to its special liability to variation, both in its morphological and in its pathogenic characters. On this subject Haffkine remarks (*Brit. Med. Jour.*, Dec. 21, 1895). "When the cholera bacillus was first discovered its properties were described with extreme precision, which helped in concentrating for a long time all studies on well-defined and carefully chosen specimens. Little by little, as the field of observation grew larger, a number of varieties have been found with characteristics differing so largely as to annihilate almost completely the original description. When we open the intestine of deceased cholera patients and investigate the microbes there, the adopted methods will bring to the surface vibrios in which the external forms, instead of the characteristic comma or spirillum, will vary between a coccus and a straight thread, the number and disposition of the cilia, the secretion of acids, the form of growth in broth, will vary; instead of giving in gelatine a discrete and well defined figure of liquefaction, the variation will extend from the complete loss of this property to a rapid dissolution of the whole medium, there will be varieties which grow luxuriantly in given media, and others which do not grow there at all; some will be phosphorescent in the dark, and others not; some will give the indol reaction, and others will be deprived of this property, and so on. The first thing to be done is to select carefully among these the most typical specimens, rejecting the others, and then to try their pathogenic power. We shall find such a divergence in strength that the extreme forms will not be believed to be the cholera species. There will be commas deprived of any virulence demonstrable on animals, and others which will kill the most resistent species. Some will be fatal to a guinea-pig at a dose of 1 100 of a culture tube, and others harmless in doses 500 times stronger. The average comma dies

out when introduced under the skin of an adult animal, others will spread in the system and give rise to a fatal septicæmia. The ordinary comma will be without effect on birds; but several specimens have been isolated, and believed to be typical, which easily killed pigeons by hypodermic or intramuscular injection. I believe to be of great value the method worked out by Pfeiffer for comparing all such varieties with one selected as typical, which he employed for the preparation of an antitoxic serum. This method will be found of efficient help in distinguishing specimens of the greatest affinity with the average cholera comma. But once such specimens are selected and their particular properties studied they begin to change from the first day they are introduced into the laboratory, and no calculation based on these studies is possible. In a case quoted by M. Metchnikoff, the proportion of the initial power of the microbe, and the strength it showed at a later trial, was as 75 to 1, the microbe having gradually sunk to 1/75 of its initial virulence." These remarks, by so great a master of the subject, whilst they indicate a way of reconciling many apparent discrepancies in matters of fact and differences in the conclusions arrived at by different bacteriologists, and whilst they indicate a key to many of the clinical features of cholera, teach us caution in accepting as proved the causal relationship of the cholera vibrio to the disease with which it is so invariably associated.

Symptoms.—An attack of cholera commences in one of two ways; either it may supervene in the course of what appears to be an ordinary case of diarrhœa, or it may come on suddenly and without any well-marked prodromal stage. During cholera epidemics, diarrhœa is unusually prevalent. It is a common observation that at such times an attack of this latter nature, after a day or two, may assume the characters of true cholera. The preliminary looseness in such cases is called the "premonitory diarrhœa." Whether this looseness is specifically related to the

typhoid character with tremor and subsultus; or the patient may sink into a peculiar torpid condition. The motions are now either greenish or like pea-soup, and may contain a larger or smaller amount of blood; at the same time they are very offensive. The reappearance of urine may be delayed from two to six days; at first scanty, high coloured, cloudy, albuminous, and containing casts, it gradually becomes more profuse, paler, and with less albumin. Though at first the urine is very deficient in urea, in uric acid, and in salts, later the quantity of these substances may exceed for a time the normal.

During the stage of reaction death may occur from a variety of complications; from pneumonia, from enteritis and diarrhœa, from asthenia, or from such effects of uræmic poisoning as coma and convulsions.

In cholera there is a considerable variety in the character of the symptoms and in their severity, both as regards individual cases and as regards different epidemics. It is generally stated that during an epidemic the earlier cases are the more severe, those occurring towards the end of the epidemic being on the whole milder. Ambulatory cases occur during all epidemics; such cases being characterised by diarrhœa and malaise merely, there is never complete suppression of urine, the diarrhœa never loses its bilious character and is unaccompanied by cramps; the attack gradually subsides without developing a subsequent stage of reaction In another set of cases, the diarrhœa may be somewhat more acute, and the stools assume the well-known rice-water appearance; but the looseness soon ceases without leading to suppression of urine, or to algide symptoms, or even to very severe cramps, and without being followed by a stage of reaction Such cases are sometimes designated "choleraic diarrhœa" or "cholerine."

A very fatal type is that known as "cholera sicca." In these cases, though there is no, or very little, diarrhœa and vomiting, collapse sets in so rapidly that the patient is quickly overpowered, as by an over-

whelming dose of some poison, and dies in a few hours without purging or any attempt at reaction. At the *post-mortem* examination the rice-water material, so characteristic of cholera, though it may not have been voided during life, is found in abundance in the bowel. Other cases die suddenly from apnœa caused, apparently, either by coagula in the right heart, or by spasm of the pulmonary arterioles, the lungs refusing to transmit the thickened blood. In certain cases, after temporary improvement, relapse may occur and is nearly always fatal Hyperpyrexia is an occasional though rare occurrence in cholera; in such the axillary temperature may rise to 107°, the rectal temperature, perhaps to 109°; these cases also are almost invariably fatal.

Cholera is apt to be followed by a variety of more or less important sequelæ, such as anæmia, mental and physical debility, insomnia, pyretic conditions, chronic enterocolitis, nephritis, different forms of pulmonary inflammation, parotitis apt to end in abscess, ulceration of the corneæ, bed sores, or in gangrene of different parts of the body Jaundice occurs at times and is said to be of the gravest import Pregnant women almost invariably miscarry, the fœtus showing evidence of cholera.

Morbid anatomy and pathology.—Rigor mortis occurs early and persists for a considerable time. Curious movements of the limbs may take place in consequence of *post mortem* muscular contractions. On dissection the most characteristic pathological appearances in cholera are those connected with the circulation and with the intestinal tract.

If death have occurred during the algide stage, the surface presents the shrunken and livid appearance already described On opening the body all the tissues are found to be abnormally dry The muscles are dark and firm; sometimes one or more of them are discovered to be ruptured—evidently from the violence of the cramps during life The right side of the heart and systemic veins are full of dark, thick, and

imperfectly coagulated blood, which tends to cling to the inner surface of the vessels. Fibrinous clots, extending into the vessels, may be found in the right heart. The lungs are usually anæmic, dry, and shrunken; occasionally they may be congested and œdematous. The pulmonary arteries are distended with blood, the pulmonary veins empty. The liver is generally loaded with blood; the gall bladder full of bile, the spleen small. Like all the other serous cavities, the peritoneum contains no fluid, its surface being dry and sticky. The outer surface of the bowel has generally a diffuse rosy red, occasionally an injected, appearance. On opening the bowel it is found to contain a larger or smaller amount of the characteristic rice-water material, occasionally blood. The mucous membrane of the stomach and intestine is generally pinkish from congestion, or there may be irregularly congested or arborescent patches of injection here and there throughout its extent. In addition, there may be seen smaller or larger points of ecchymosis in, or under, the mucous membrane. The changes in the alimentary canal are most marked at the lower end of the ileum, where Peyer's patches and the solitary glands may be seen to be congested and swollen. In some instances the bowel is pale throughout; in many the mucous membrane has a sodden, pulpy appearance from exfoliation of epithelium—possibly a *post-mortem* change, occasionally, especially towards the lower end of the ileum, a croupous exudation is met with. The mesenteric glands are congested. The superficial veins of the kidneys are full: the medullary portion is much congested, the cortical portion less so; the tubules are filled with granular matter, the epithelium is cloudy, granular, or fatty, and, at a later stage, may be shed. The bladder is empty and contracted. Nothing special is to be noted in the nervous system.

If death have occurred during the stage of reaction, the tissues are moist; the venous system is less congested; the lung probably congested and

œdematous, perhaps inflamed. Very probably there are evidences of extensive enteritis.

Microscopical examination of the contents of the bowel during the acute stage of the disease discovers, in most instances, the comma bacillus. Usually it is in great abundance; occasionally in what is almost a pure culture. Sections of the intestine show the bacillus lying on and between the epithelial cells of the villi and glands. In no other organ or tissue of the body is the bacterium to be found. Therefore, assuming that the comma bacillus is the cause of cholera, we must conclude that the clinical phenomena are not the result of a septicæmia; but that they arise, either from a local irritation produced by the bacillus, or from some toxin which it generates in the bowel and which is absorbed, or from a combination of these factors.

That the cholera vibrio is a powerful irritant is shown by the effect produced locally by a hypodermic injection of a virulent culture. When so injected, not only does it give rise to local œdema but, unless special precautions are taken, it causes necrosis of the tissues and extensive ulceration at the seat of injection. It is conceivable, therefore, that when in the course of the naturally acquired disease the bacilli proliferate in the bowel, they or their products act as an irritant to the mucous membrane and so provoke the hypercatharsis, and the consequent dehydration of the tissues, which are the dominating features of the disease. On the other hand, the hypodermic injection of cholera vibrio cultures is followed by smart febrile movement lasting from one to three days, evidencing the presence of a febrogenetic toxin capable of producing constitutional symptoms. This fact, together with the rapid and intense prostration which, in some instances of natural cholera, appears to be out of all proportion to the amount of catharsis present, suggests that in a measure the lethal effects of the vibrio are attributable, not alone to the drain of fluid from the blood and tissues but also to the absorption of a

cholera toxin from the intestine. It is somewhat strange, however, if this toxin be anything more than a subsidiary element in the production of the symptoms in most instances of the naturally acquired disease, that catharsis is not one of the effects of the hypodermic introduction of the vibrio, and that fever is not an earlier and more prominent symptom in natural cholera. The modern tendency is to regard the clinical phenomena as the result partly of local irritation and partly of a toxæmia, variation in the proportional intensities of the various clinical elements depending on the degree of virulence of the particular strain of microbe introduced, and on the circumstances and idiosyncrasy of the patient.

Diagnosis.—During the height of an epidemic the diagnosis of cholera is generally an easy matter; the profuse rice-water discharges, the collapse, the cold clammy skin, the cyanosis, the shrunken features, the shrivelled fingers and toes, the feeble, husky, hollow voice, the cold breath, the cramps and the suppression of urine, together with the high rate of mortality, are generally sufficiently distinctive. But in the first cases of some outbreak of diarrhœa, which may or may not turn out to be cholera and the true nature of which for obvious reasons it is of importance to determine, diagnosis may not be so easy. Symptoms resembling true cholera may supervene in the course of an ordinary severe diarrhœa, and are very usual in cholera nostras, in mushroom poisoning, in ptomaine poisoning, in the early stages of trichinosis, and in a certain type of pernicious malarial fever. In none of these, however, is the mortality so high as in cholera; it may be laid down, therefore, that epidemic diarrhœa attended by a case mortality of over 50 per cent. is cholera.

In other forms of diarrhœa it is rare for the stools to be persistently so absolutely devoid of biliary colouring matter as they are in cholera. A careful inspection of the stools sometimes yields valuable information in other ways. Thus in mushroom

poisoning, fragments of the mushrooms which caused the catharsis may be seen; in trichinosis, the microscope may detect the adult trichina. In choleraic malarial attacks the presence of the plasmodium in the blood, the periodicity of the symptoms, their amenability to quinine, together with the character of the prevailing epidemic, generally combine to guide to a correct diagnosis.

The detection of the comma bacillus in the stools is now regarded as a positive indication of cholera. It would be rash, however, to affirm that a negative result from bacteriological examination of a single case is conclusive against its being cholera. Moreover, it must be borne in mind that such examinations to be trustworthy have to be made by a skilled bacteriologist. According to Kanthack and Stephens, the following were the methods of bacteriological diagnosis practised by Klein during the threatened epidemic in 1893

"*Method* 1.—A flake from the dejecta is placed in peptone broth and incubated at 37° Cent. In twenty four hours an abundant crop of vibrios is found on the superficial layers of the broth. This pellicle consists of a practically pure culture, or, at any rate, is a culture which easily allows of pure sub-cultures being obtained.

"*Method* 2. A flake is placed in sterile salt solution or broth; it is shaken up, and from this gelatine or agar tubes are inoculated, and plates are made. In agar plates incubated at 37° Cent. numerous colonies may be found in twenty to thirty hours. In the gelatine plates, after two to three days' incubation at 20 to 22 Cent. numerous typical colonies can be got.

"*Method* 3.—A flake is placed directly into Dunham's peptone salt solution (1 per cent. peptone, 0·5 per cent. sodium chloride), or the Dunham's solution is inoculated after previous dilution of the material. The peptone solution, after six, eight, to ten hours' incubation at 37° Cent. shows a definite turbidity, due to the rapid growth of the comma bacilli; and the

cholera-red reaction may be obtained. For speedy diagnosis this method is most valuable; in six to twelve hours, or, at latest, in sixteen hours, comma bacilli can be found in the superficial layers of the peptone solution, so that in twenty four hours pure cultures and the cholera-red reaction can be obtained in secondary peptone tubes. Also, a positive result may be obtained by this method in cases in which the microscopical examination has failed to give definite evidence of the presence of vibrios."

The first two methods are applicable to those instances in which microscopical examination of the stools shows crowds of comma bacilli. Method 3 is specially applicable to those stools in which comma bacilli are in very small numbers.

Mortality.—The average case mortality in cholera amounts to about 50 per cent. Some epidemics are more deadly than others. The mortality is greater at the earlier stages than at the later stages of an epidemic. To the old, the very young, the pregnant, the subjects of grave organic disease -particularly of the liver, kidneys, and heart—the dissipated, the underfed, and the feeble, the danger is very great.

Quarantine prevention. Theoretically, quarantine should be an efficient protection against the introduction of cholera into a community; practically, it has proved a failure. Unless they are stringent and thoroughly carried out, quarantine regulations can be of little use. Unfortunately, the temptation to evade such regulations is in proportion to their stringency. It is impossible to secure the absolute honesty and efficiency of every individual in a large body of men charged with the carrying out of the details of any system entailing great personal inconvenience and loss to travellers and merchants. Therefore, if the strength of the quarantine chain is to be measured by its weakest link, the chain must be weak indeed, as a very slight acquaintance with its working will prove. Even if the utmost care, intelligence, and honesty succeed in excluding

individuals actually suffering from cholera, or likely within a reasonable time to suffer from cholera, there is yet no guarantee that the germ of the disease may not be introduced. Koch and others have shown that sometimes the dejecta even of individuals apparently in good health and who have not suffered, or who may not subsequently suffer, from choleraic disease, may yet contain, and for some time continue to contain, the cholera vibrio. If the cholera vibrio be the germ of cholera, then such healthy, vibrio-bearing individuals may well suffice to start an epidemic. It is impossible, short of absolute and complete isolation, for any practicable system of quarantine to deal efficiently with such cases.

So far from ordinary quarantine proving a defence against cholera, it may actually increase the risk of an epidemic. This it does by fostering a false sense of security, leading to the neglect of those well-proved guarantors of the public health—domestic, municipal, and personal cleanliness, and a pure water and food supply.

The system to which Great Britain apparently owed her immunity during recent epidemics on the continent of Europe is a practicable one, and, in civilised conditions, seems to be an efficient one. Under this system only ships carrying, or which had recently carried, cholera patients were detained; and even these merely till they could be thoroughly disinfected. Thus inconvenience and loss to travellers and merchants were small, and the temptation to conceal cases of the disease, or to evade regulations, was proportionately minimised. Any cholera cases were isolated in suitable hospitals, the rest of the crew and passengers, although supervised for a time, being given free pratique. At the same time, attention was not diverted from the sanitation of towns, especially of seaports; this was the measure mainly relied on. Suspicious cases occurring on shore were at once reported to the sanitary authorities and promptly dealt with, fomites being destroyed or disinfected at

as little cost and inconvenience to individuals as possible Every endeavour was made to prevent fæcal contamination of the public water supply.

Of late years in India effort is being directed much on the same lines, attention being given to sanitation rather than to quarantine. During the great religious festivals the sanitary condition of the devotees is looked after so far as practicable, special care being given to provide them with good drinking and bathing water. Many of the large Indian towns now enjoy an abundant and pure water supply, and civilised systems of night soil conservancy and other important sanitary measures are being gradually introduced, in the case of more than one great city, with the most gratifying results.

Among the troops in India, on the appearance of cholera in their neighbourhood special protective measures are promptly instituted, elaborate directions having been drawn up for the guidance of medical officers. For an account of these regulations the reader is referred to the Annual Report of the Sanitary Commissioner with the Government of India for 1895, Appendix, p. 189.

Incubation period.—All quarantine and protective systems must take cognisance of the fact that although cholera may declare itself within a few hours of exposure to infection, it may also do so till as late as ten days. Three to six days may be set down as the usual duration of the incubation period.

Anti-choleraic inoculations. — In 1885, during an epidemic of cholera in Spain, Ferran instituted a system of prophylactic inoculation. He injected hypodermically ordinary laboratory cultures of the cholera vibrio obtained directly from cholera corpses. No attempt was made to regulate or standardise in any way the virulence of the cultures. The results were not encouraging. As accidents were frequent, the Government put a stop to the practice

In 1893 (*Brit. Med. Jour.*, Feb. 11th, 1893) Haffkine, after elaborate experiments on the lower

animals, commenced a system of anti-choleraic vaccinations, using a pure virus of a fixed and known strength. This virus he prepared by passing the cholera vibrio through a series of guinea-pigs by means of intra-peritoneal injections. In this way the microbes were increased in toxicity to a definite point, beyond which their virulence could not be augmented. Cultures so prepared gave rise not only to a general but also to a local reaction, the latter being so severe that it generally ended in extensive sloughing and ulceration. To avoid this undesirable result, a milder vaccine was prepared by cultivating the strong vaccine in artificial media at a temperature of 39 Cent., and in an atmosphere kept constantly renewed. By first injecting under the skin of animals this milder vaccine, it was found that such a measure of protection was conferred that subsequent injection of the strong virus was no longer followed by a local reaction of such severity as to cause sloughing or ulceration. Having satisfied himself that the subcutaneous injection of these two vaccines conferred immunity against the cholera vibrio in the lower animals, Haffkine proceeded to use them in man on a large scale in India, and with the approval and aid of the Government. Up to 1895 70,000 injections of living cholera bacilli had been made in 43,179 individuals. In no instance did any bad result ensue. While admitting that the value of his method has not been fully proved, Haffkine claims that the results are sufficiently encouraging to justify a continuation of these inoculations on a larger scale. The symptoms they produce are fever, transient œdema, and tenderness at the seat of injection, the first evidence of constitutional disturbance appearing from two to three hours after the injection is made. The fever and general indisposition last from twenty-four to thirty six hours, the local symptoms gradually disappearing in from three to four days. The symptoms following the second injection—made from three to four days after the first—are generally more marked but of shorter

duration. The microbes injected die. It is the substances set free at their death which confer the immunity, for it is found that carbolised cultures—that is, dead vibrios—produce the same immunising and constitutional effect, though in a somewhat milder and probably less permanent degree. How long the immunity conferred by these injections endures has not been definitely settled. Full details of Haffkine's methods and technique are given in the *Brit. Med. Jour.* of Feb. 4th, 1893, and in the *Indian Medical Gazette* of Nov., 1896.

Personal prophylaxis.—During cholera epidemics great care should be exercised to preserve the general health; at the same time, anything like panic or apprehension must be sedulously discouraged. Fatigue, chill, excess—particularly dietetic or alcoholic excess—are to be carefully avoided. Visits to cholera districts should be postponed if possible, seeing that the newcomer is specially liable to contract the disease. Unripe fruit, over-ripe fruit, shell-fish, food in a state of decomposition, and everything tending to upset the digestive organs and to cause intestinal catarrh are dangerous. Melons, cucumbers, and the like deserve the evil reputation they have acquired. Purgatives—particularly saline purgatives—unless very specially indicated, should never be taken at these times. All drinking water, and all water in which dishes and everything used in the preparation and serving of food are washed, should be boiled. Filters—except perhaps the Pasteur-Chamberland filter—are not to be relied on; in most instances they are more likely to contaminate the water passed through them than to purify it. A good plan in a household, or in public institution, is to provide for drinking purposes an abundant supply of weak tea or lemon decoction, the supply being renewed daily; such a plan insures that the water used in the preparation of the drink has been boiled.

Diarrhœa occurring during cholera epidemics should be promptly and vigorously treated.

Treatment. — During cholera epidemics it is customary to establish depôts where sedative and astringent remedies are dispensed gratuitously for the treatment of diarrhœa. Experience seems to encourage the belief that by such means incipient cholera may be aborted during the stage of premonitory diarrhœa. Of the various drugs used with this view, chlorodyne, or chlorodyne and brandy, is the most popular. Lead and opium pill; chalk, catechu and opium mixture; compound kino powder; aromatic powder of chalk and opium; a pill of opium, asafœtida and black pepper; dilute sulphuric acid and laudanum are among the drugs more commonly employed for this purpose. Whether true cholera can be cut short in this way or not, it is certainly in the highest degree advisable at such a time to neglect no case of diarrhœa; but to insist on rest, warmth, and the greatest prudence in feeding in all cases of intestinal catarrh or irritation.

Many plans of treatment, based on theoretical considerations, have been advocated from time to time; so far, however, none of them has proved of material service in true cholera. The eliminative treatment advocated by Dr. George Johnson; the spinal ice-bag recommended by Chapman; various antiseptic methods directed to the destruction of the vibrio in the intestinal canal; drugs designed to counteract the physiological effects of the cholera toxins, as chloroform, atropine, nitrite of amyl, and nitro-glycerine may be mentioned as belonging to this category of remedies.

Practically, the only treatment of any proved value in cholera is the purely symptomatic and expectant one. If our efforts have failed to counteract the premonitory diarrhœa, attention should be given to maintaining the patient in as favourable a condition as possible to struggle against the poison of the disease. He should be kept strictly in the horizontal position, in a warm bed, and in a well-ventilated but not too cold room. His thirst should

be treated by sips of iced-water or of soda-water, or champagne, or brandy and water, copious draughts provoke vomiting Cramps may be relieved by gentle frictions with the hand or with ginger-root, by a small hypodermic injection of morphia, or, these failing, by short chloroform inhalations. The surface of the body should be kept dry by wiping it with warm dry cloths, and the surface heat maintained by hot water bottles or warmed bricks placed about the feet, legs, and flanks. The patient must not be allowed to get up to pass his stools, a warmed bed-pan being provided for this purpose. All food should be withheld while the disease is active.

If the pulse fail or disappear at the wrist, stimulants by the mouth, or, if there is much vomiting and these do not appear to be absorbed, hypodermic injections of ether or brandy may be given. No improvement ensuing, intravenous injection of saline fluid may be had recourse to. A suitable injection may be quickly prepared of common salt sixty grains, carbonate of soda sixty grains, boiled water one quart. Of this, from one to three quarts at a temperature of 100° Fahr. may be slowly injected by gravitation into a vein, the effect being carefully watched. The pulse can generally be quickly restored temporarily by this means and life prolonged, possibly in a few instances saved, too often, however, the fluid so introduced rapidly escapes by the bowel and collapse once more sets in Dr Cox, of Shanghai, has had some encouraging results from continuous, prolonged, slow, intravenous injection of saline fluid, the fluid gravitating from a vessel placed two and a half feet above the level of the patient's arm. The flow is kept up for several hours, and as long as it is deemed that there is any risk of collapse (*China Med. Missionary Jour.*, June, 1897).

During the stage of reaction, should purging persist, large doses of salicylate of bismuth with a little opium may prove of service. In these circumstances massive rectal injections of tannin one ounce

gum arabic one ounce, warm water one quart, are of use. If the secretion of urine is not quickly restored, large hot poultices over the loins, dry cupping of the same region, and the judicious use of bland diluents should be had recourse to. Stimulating diuretics are dangerous. Retention of urine must be inquired about, and the region of the bladder frequently examined, and, if necessary, the catheter employed. In the event of constipation, purgatives must be eschewed and simple enemata alone used.

In cholera convalescents the diet for a time must be of the simplest and most digestible nature—diluted milk, barley-water or rice-water, thin broths, meat juice, and so forth—the return to ordinary food being effected with the greatest circumspection.

Cholera typhoid must be treated much as an ordinary enteric fever.

CHAPTER XVIII.

DYSENTERY.

Definition.—A term applied to what is probably a group of diseases whose principal pathological feature is inflammation of the mucous membrane of the colon, and whose leading symptoms are pain in the abdomen, tenesmus, and the passage of frequent small stools containing mucus and blood. In some instances the disease is communicable.

Geographical distribution.—From time to time forms of dysentery have extended as epidemics of great severity over vast tracts of country. These great epidemics, or such of them as have been recorded, have been confined principally to temperate latitudes, and do not specially concern us here.

In respect to geographical distribution and certain epidemiological points, tropical dysentery bears a close resemblance to malaria. Like malaria, although dysentery is found in temperate climates in them it is, with exceptions, a comparatively rare and mild affection. Like malaria, as we approach the Equator dysentery tends to become more common, and in type more severe. Like malaria, it is endemic in certain spots, where it often appears in sporadic form, and, at times, in limited local epidemics. Like malaria, it may extend beyond these endemic spots and involve more extensive tracts of country. Like malaria, it appears to have a predilection for low-lying, damp places; and, like malaria, when occurring in temperate climates it is most prevalent in the late summer, or in early autumn. Like malaria, it tends to disappear on the cultivation, drainage, and improved sanitation of a

country. Furthermore, the two diseases often occur in the same places and at the same time. They may even concur in the same individual; and one disease seems to predispose to the other.

To this extent these two diseases resemble each other; nevertheless, though they have many points in their epidemiology and in their geographical distribution in common, they are pathologically totally distinct and independent affections, with different causes, different lesions, and requiring different treatment. Moreover, there are many places where dysentery is common and where malaria is unknown, and, though very much more rarely, *vice versâ*.

Symptoms. — In ordinary cases the leading symptoms of dysentery are those of inflammation of the great intestine—namely, griping, tenesmus, and the passage of frequent loose, scanty, muco-sanguineous stools. It commences in various ways —insidiously, or suddenly; or it may be grafted, as it were, on some general affection such as scurvy or malaria, or on some chronic disease of the alimentary canal, as sprue. It may assume acute characters, or from the outset the symptoms may be subdued and of little urgency. As a rule, the symptoms are proportioned to the extent of the disease, but they are not necessarily so. In certain cases they may be extremely urgent and in apparent disproportion to the area of bowel affected; or they may be, in comparison to the extent and the degree of the anatomical lesion, disproportionately trifling; or they may be altogether absent, even when the colon is extensively diseased. There is, therefore, endless variety in the character, urgency, and significance of the symptoms of dysentery. As a general rule, the nearer to the rectum the lesions, the more urgent the tenesmus; the nearer to the cæcum, the more urgent the griping. These two symptoms, together with the presence of points of localised tenderness, form, in the majority of cases, a fair guide to the location and extent of the lesions.

Catarrhal dysentery.—A common history to receive from a patient is that for some days he, or she, had suffered from what was supposed to be an attack of ordinary diarrhœa. The stools, at first copious, bilious and watery—perhaps to the number of four or five in the twenty-four hours—had latterly, and by degrees, become less copious and more frequent, less feculent and more mucoid, their passage being attended by a certain and increasing amount of straining and griping. On looking at what was passed, the patient had discovered that now there was very little in the pot except mucus tinged, or streaked, or dotted with blood; a tablespoonful, or thereabouts, being passed at a time. By degrees the dysenteric element entirely supplanted the diarrhœa; so that when seen by the physician the desire to go to stool has become almost incessant, the effort to pass something being accompanied by perhaps agonising griping and tenesmus. The patient has hardly left the stool before he has a call to return to it, and he may be groaning and sweating with pain and effort. The suffering is sometimes very great; nevertheless, with all this suffering, there is very little fever, the thermometer showing a rise of only one or two degrees, rarely more.

In another type of case the incidence of the dysenteric condition is much more abrupt. Within a few hours of its commencement the disease may be in full swing. The stools, at first feculent, soon come to consist of little save a yellowish, greenish, or dirty brown mucus—blood-tinged or streaked and dotted with little hæmorrhages. Very soon the desire to stool becomes increased, the griping and tenesmus being accompanied, perhaps, with most distressing dysuria. The patient is glued, as it were, to the commode. Fever is absent or inconsiderable. The tongue soon becomes white or yellow-coated; there may also be thirst; very generally anorexia is complete.

In either case, after perhaps four, five, or six days, the urgency of the symptoms may gradually diminish

and the acute stage taper off into a subacute or chronic condition; or it may terminate more quickly in perfect recovery.

Ulcerative dysentery.—Should, on the contrary, the disease advance, the urgency of the symptoms shows hardly any abatement; the stools become very offensive, and now contain, besides blood, large or small shreddy, ash-coloured, stinking sloughs. This may go on, better or worse, for days or weeks. Recovery from this condition is a slow process, as the presence of sloughs in the stools indicates the existence of deep ulceration which must necessarily take some time to cicatrise. Such a condition tends to drift into that most dangerous and most distressing complaint, chronic dysentery, relapsing and improving during many months or even years; and causing, if severe and prolonged, great wasting, pain and misery.

Gangrenous dysentery.—What is known as gangrenous dysentery is, symptomatically, but an aggravated form of acute ulcerative dysentery. Instead of being mucoid, the stools come to consist of a sort of dirty water, like the washings of flesh. On standing, they deposit a grumous, coffee-ground-looking material, and they stink abominably. Now and again sloughs of every shape, size, and colour, from ash-grey to black, are expelled. Sometimes tube-like pieces, evidently rings of mucous membrane which have been cast off *en masse*, are discharged. In such cases the patient rapidly passes into a state of collapse. He sweats profusely; the features, the extremities, and even the whole body, are cold and pinched as in the algide stage of cholera; he may vomit from time to time, and the belly may become distressingly tympanitic. In this condition there is usually a persistent and worrying hiccough. Low muttering delirium sets in; the pulse becomes small and running, and the patient rapidly sinks. Recovery is extremely improbable. Nevertheless, such cases have recovered, and must not necessarily be despaired of.

Hæmorrhage. Whenever in dysentery sloughs separate, hæmorrhage is always possible. Sudden collapse may occur from this cause, even in otherwise mild cases. As in typhoid, the occurrence of hæmorrhage is more or less of the nature of an accident, depending, as it does, on the position of the sloughing sore in relation to an artery, of course, the more extensive and the deeper the sloughing, the greater the liability to hæmorrhage.

Perforation.—Another grave, though fortunately rare, accident in the course of dysentery, is the occurrence of perforation. Should this unhappily take place, and if the patient survive the shock of an extensive extravasation into the peritoneum, symptoms of peritonitis will supervene and rapidly prove fatal.

Intussusception.—Intussusception is also an occasional occurrence, especially in children, not always readily recognised. A sudden increase of pain, increased straining, entire absence of fæcal matter from the stools, vomiting, and perhaps the presence of a tumour in the rectum, might lead one to suspect this accident.

Tenderness; thickening. — In most cases of dysentery there is a considerable amount of tenderness of the abdomen; and if the disease be of some standing a certain amount of thickening may be felt along the track of the colon, particularly over the sigmoid flexure.

Hepatitis. In acute dysentery the liver is usually distinctly enlarged and may be tender. It sometimes happens that attacks of hepatitis seem to alternate with attacks of dysentery; or, rather, that hepatitis increasing, dysenteric symptoms decrease and *vice versâ*. These are always very anxious cases, and too often eventuate in the formation of an abscess or multiple abscesses in the liver, in the latter event they almost necessarily prove fatal.

Pathognomonic symptoms.—No two cases of dysentery are exactly alike. In epidemic dysentery,

which is usually of a more severe type than the sporadic form, the individual cases have a general resemblance to each other. In all varieties the leading symptoms are the same—frequent discharge of muco-sanguinolent stools, tenesmus, griping, and, usually tender abdomen. In the presence of these symptoms, with or without fever, particularly if the disease be epidemic at the time, a diagnosis of dysentery is probably correct.

Mortality.—Although every now and again cases are met with which prove directly fatal from rapid exhaustion, from hæmorrhage, or from perforation; and though some epidemics exhibit a malignancy which, fortunately, is not very common, the direct and immediate mortality from this disease is, under modern methods of treatment, not very high. In India, the case mortality in dysentery among Europeans ranges from 3 to 22 per cent.; among natives, about 37 per cent. In Egypt, Griesinger stated it at 36 to 40 per cent. In Japan, Scheube places it at 7 per cent. These figures are of little value, as so much depends on the place, the type of the epidemic, and the range of cases covered by the statistics. There was a time when, under a spoliative treatment by bleeding and calomel, dysentery proved a very fatal disease indeed. Even now, in the presence of scorbutus, famine, the stress of war, and similar conditions, whenever dysentery becomes epidemic in a community, it is apt to claim a large number of victims.

Sequelæ more dangerous than the disease.—As a rule, under modern treatment, it is the sequelæ of the disease that we have to fear rather than the disease itself. The chronic ulceration, the scarring, thickening, and contractions of the gut, are conditions which cannot be remedied; and which too often, after months or years of suffering, lead to intestinal obstruction, or, very frequently to a general atrophy of the glandular system of the entire alimentary tract, wasting, and fatal asthenia. Such patients hardly ever pass a healthy motion; they

are troubled with chronic indigestion; they pass their food unaltered; they have recurring attacks of diarrhœa; they are flatulent; their tongues are red, often ulcerated and tender; they develop the condition known as "sprue," and, sooner or later, almost invariably succumb.

Liver abscess.—Much more frequent in its occurrence than these, and much more rapidly fatal, sometimes accompanying or quickly following dysentery, more often showing itself after months of comparative good health and when dysenteric symptoms had long ceased to trouble the patient, had perhaps been forgotten even, there is suddenly sprung on us the gravest of all the sequelæ of this disease—the patient gets abscess of the liver. This important subject is specially dealt with elsewhere in this volume (p. 343).

Morbid anatomy and pathology. — We were able to study the cognate subject of malaria to a certain extent scientifically; at all events, we could point out its germ or cause, and, in a measure, indicate the way in which this germ produced pathological effects. Unfortunately, in the case of dysentery this cannot be done. Although in many instances the specific nature of the disease is not to be doubted, the specific body or germ has not been indicated with anything like certainty. Many bacteria have been incriminated—the bacillus coli commune, a bacillus dysenteriæ, staphylococcus aureus and s. albus, etc. In one form of dysentery claims have been advanced for regarding the amœba coli as the germ. Up to the present all or any of these claims, whether for bacteria or for protozoa, are still very far from being established.

In treating of the pathology of dysentery, therefore, we cannot begin by describing the cause; we can describe the effects, and only speculate about their cause or causes.

The term dysentery includes, probably, several diseases.—There is good reason to believe that the

term "dysentery" includes not one but several distinct diseases. We know that the symptoms grouped under this word are apt to differ in intensity and character in different places and in different epidemics. Some forms of the disease run a more or less definite course, and then terminate for good. Other forms exhibit a remarkable disposition to relapse. The dysentery of certain tropical countries, as the East Indies, is prone to eventuate in abscess of the liver; that of temperate climates and certain tropical countries, as the West Indies (excepting one or two of those epidemics of which we have trustworthy accounts) is seldom succeeded or accompanied by hepatic suppuration. These and other circumstances seem to point to radical differences in the several forms—differences of cause as well as differences of symptoms, course, and sequelæ. It is well, therefore, to regard the term "dysentery" as but the name of a symptom or group of symptoms indicating an inflamed condition of the colon—much in the same way as we regard diarrhœa, cough, or fever as symptomatic merely of disease, and not as indicating a single and well-defined disease. Dysentery simply means inflammation of the colon. There may be many kinds of inflammation of the colon.

Catarrhal dysentery.—It is unreasonable to suppose that those cases which, either spontaneously or in consequence of treatment, subside in a few days, advance further than a state of catarrhal inflammation. In such cases it is reasonable to suppose that the pathological condition consists only, or mainly, in congestion or in catarrhal inflammation; that here and there, or throughout its extent, the mucosa and, perhaps, submucosa are slightly swollen, red, injected; and that the surface of the former is softened, perhaps eroded, and covered with a blood-streaked glairy mucus of the same character as that which appears in the stools.

Ulcerating dysentery.—Cases of catarrhal dysentery rarely die; the exact conditions of the mucous

membrane, therefore, in these cases can only be conjectured. It is otherwise, however, in the severer forms of the disease. When such cases come to the *post-mortem* table, the mucous membrane of the large intestine and, very frequently, a foot or two of the lower end of the ileum are found to be thickened, congested, inflamed, speckled perhaps with ecchymoses, œdematous, and more or less riddled with ulcers of various sizes, shapes, and depths. It is found, as a rule, that the brunt of the disease has fallen on the sigmoid flexure and descending colon; not infrequently, however, the lesions are equally, if not more, advanced in the cæcum and ascending colon. On the whole, the transverse colon, though often seriously involved, is so to a less extent than one or other of the parts mentioned, or than the hepatic and splenic flexures.

The dysenteric ulcer varies in size from a punched-out-looking sore the size of a pea, or even less, to a patch several inches in diameter. As a rule, in the earlier part of the acute stage, the ulcers tend to follow the folds of the mucous membrane, the free borders of which are the parts most liable to implication. The edges of the sores are ragged and undermined, the floor is sloughy and grey. There may be considerable thickening of the edges and base of the ulcer, with peritoneal adhesions. The appearance of the ulcer suggests that it extends by a process of burrowing in the submucosa, the superjacent mucous membrane sloughing or disintegrating in consequence of the subjacent destruction of its nutrient vessels. This burrowing may extend for a considerable distance beyond the apparent margin of ulceration; so much so that long, suppurating, fistulous tunnels may connect one ulcer with another. In this way large patches of mucous membrane come to be undermined, and subsequently to slough away. Sores so formed are necessarily ragged and irregular in outline, and may even surround pieces of comparatively healthy mucous membrane. The floor of the active dysenteric ulcer may

be, and generally is, formed of a sloughy material lying on the muscular coat; but the sore may penetrate deeper than this, and include the muscular coat itself, and even the serous membrane. The largest ulcers are generally found in the sigmoid flexure and descending colon; they are also frequently, though more rarely, found in the cæcum, the magnitude of the lesions diminishing as we trace the bowel upwards or downwards, as the case may be.

Along with the ulceration there is intense congestion of the non-ulcerated parts of the mucous membrane. In places there may be œdema of the submucosa; there may be small abscesses even which elevate the mucous membrane; and there may also be distension of the solitary follicles by a mucoid or purulent material. In some instances a large portion of the mucous membrane may be seen to have died *en masse* and become gangrenous. In such, extensive sloughs may be thrown off as a sort of tube, apt to be mistaken during the lifetime of the patient for a diphtheritic cast of the bowel.

The primary lesion.—Such, briefly, is a description of the principal lesions found in the acute stage of fatal cases of dysentery. There is general agreement among pathologists about these; but there is very great discrepancy of opinion as to the exact nature of the primary and essential lesion. Some maintain that the starting-point of the disease is in the solitary follicles which, becoming distended by a specific exudation, afterwards slough, and form the starting-point for a spreading ulcer. Other pathologists regard the primary lesion as being altogether independent of the glandular structures of the mucous membrane. They hold that, in consequence of the irritation produced by the specific cause of dysentery, an exudation is thrown out on to and into the continuity of the mucous membrane itself; a dry eschar is formed of this, the implicated piece of tissue being subsequently got rid of, very much in the same way as the slough forming the core of an ordinary boil.

Another primary lesion described is the small abscess, already alluded to as elevating the mucous membrane and projecting into the lumen of the gut; these minute, pimple-like abscesses consist of a collection of a sort of gummy pus. After a time a minute opening forms at the apex of the little swellings, through which the contents may be expressed, and, as already stated, it is this opening which they say forms, on enlarging, the specific ulcer of dysentery. Assuming that there are several specific causes for dysentery, it is to be expected that the corresponding primary lesions differ; that whilst one causes a suppurative or gangrenous lesion, another may produce a croupous or diphtheritic one which, in time, may also end in ulceration.

Healing process.—The dysenteric ulcer heals partly by contraction, partly by the formation of a very thin scar tissue—scar tissue which, besides contracting, is apt to become pigmented. Lost glandular structures are never reproduced. Owing to the constant peristaltic movement of the gut, and the passage of fæces over the face of the healing ulcer, cicatrisation, as might be supposed, is a slow process, and one prone to interruption by recurring attacks of inflammation.

Lesions in chronic dysentery.—In chronic dysentery the ulcers are usually smaller and less numerous than in the acute disease. They are also less ragged in outline, tending to become circular in shape and to acquire thickened rather than undermined edges. Cicatricial bands and contractions may narrow the lumen of the gut, whose functions are still further hampered by thickening, or by adhesions which unite and bind it to neighbouring organs. Dilatation above the seat of cicatricial stricture is liable to ensue. In chronic dysentery large patches of the bowel, and even the ulcers themselves, may be pale and anæmic; whilst, at the same time, other patches of the gut are congested. Some parts may be thickened and contracted; others, again, may be thinned and dilated, the glandular structures being atrophied.

Polypoid growth.—Some time ago I attended a case of chronic relapsing dysentery in which the mucous membrane—at all events of the rectum and descending colon—was covered with enormous numbers of polypoid growths of considerable magnitude, some of them at their free ends being as large as the tip of the little finger. The growths had pedicles one to two inches in length. During life these polypoid bodies appeared in the stools, often in great number, looking like so many mucilaginous seeds. Similar cases are occasionally met with.

Liver; mesenteric glands.—In by far the majority of cases of acute dysentery, the liver is hyperæmic and swollen. In about one-fifth of the cases of Indian dysentery which come to the *post-mortem* table, the liver is the seat of single or multiple abscess. In chronic dysentery this organ may be atrophied; very generally it is the subject of fatty degeneration.

In acute cases the mesenteric glands are enlarged, soft, and congested; in chronic cases they are enlarged, hard, and pale. None of the other viscera are characteristically affected. Abscess is sometimes discovered about the rectum. If perforation has occurred, there may be signs of commencing peritonitis.

Ætiology.—Our knowledge of the cause of dysentery is of a most fragmentary and unsatisfactory character. Probably the several specific causes or germs of colitis have their action supplemented by the ordinary bacteria of suppuration and ulceration, which find their opportunity in a tissue weakened by, what may be regarded as, the more specific cause or causes of dysentery. It must be with the mucous membrane of the bowel, in this respect, as it is with the skin of the surface of the body. There are many causes for eczema and many secondary germs which proliferate on, and further irritate, an eczematous skin; so with the intestinal mucosa.

Amœba coli.—Lately, certain observers—particularly Kartulis, Councilman, Lafleur, Kruse, and Pasquale—have endeavoured to make out that there

is a distinct type of dysentery associated with the presence of the amœba coli in the stools. According to these authors, this type of the disease is caused by the amœba, and they designate it "amœbic dysentery." As distinguished from other forms of the disease, its principal clinical characteristics are said to be chronicity, relapses alternating with periods of comparative quiescence, great liability to the formation of abscess

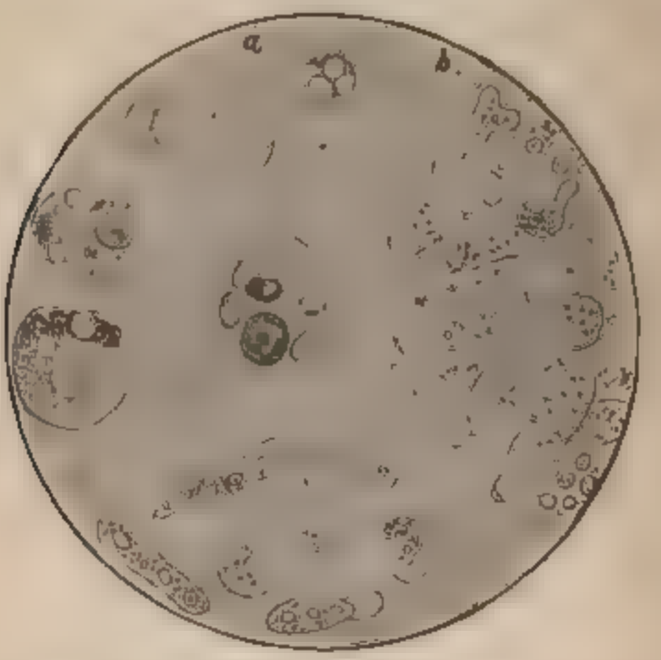

Fig. 28. Amœba coli.

a, Amœba dysenteriæ fixed and stained (Councilman); b, a, dysenteriæ in stool (after Losch, Virchow's "Arch v," Bd. 65).

of the liver, and the presence of the amœba in the stools.

When present, the amœba (Fig. 28) is generally easy to find. All the preparation necessary is to pick out a small fragment of stool shortly after it has been passed, preferably a piece of flocculent mucus, and then to lay this on the slide, and compress it sufficiently under the cover-glass to form a fairly transparent film. In warm weather a warm stage is not required; but in cold weather it is well, until the observer has become by practice familiar

with the appearance of the parasite in its passive condition, to warm the slide. This, in the absence of more elaborate apparatus, may be conveniently done by placing the slide on a copper or tin plate with a hole cut in it to allow the transmission of light. Such a warm stage should be provided with a long arm to the end of which a spirit lamp is applied, care being taken not to raise the temperature of the slide above blood heat. Search is then made with a half-inch objective. The amœba, which is a clear body, having a very faint, often hardly perceptible, greenish tinge, some three to five times the diameter of a red blood-corpuscle, is recognised by its movements, which closely resemble those of the ordinary fresh-water amœba. It consists of a somewhat granular endosarc surrounded, when active, by a very clear ectosarc. A nucleus may sometimes be detected in the endosarc, as well as one or two non-contractile vacuoles, and, generally, various extraneous bodies such as blood-corpuscles, bacteria, and so forth, which the amœba has included. As the temperature of the slide approaches blood heat the amœba sends out and retracts rounded pseudopodia. These when first protruded consist of ectosarc only; but when the clear protrusion of ectosarc has been extended a little way the endosarc is seen suddenly to burst, as it were, and flow into it. If the temperature of the slide be allowed to fall below 75° Fahr. the parasite assumes a sharply-outlined spherical form and remains quite passive until the slide is again warmed up, when the creeping movement may be resumed. In certain specimens heat fails to induce movement, the amœba remaining spherical and passive as if encysted. The parasite will keep alive on the slide and exhibit movement for an hour or two.

There can be no question as to the occurrence of this parasite in dysentery, but it is difficult to say what may be its exact significance in relation to the disease. It is found not only in the mucus lying on

or thrown off by the inflamed bowel, but also in the sloughs on the ulcerated surface and even, according to Kartulis, Councilman and Lafleur, in the tissues constituting the base and sides of the ulcer, and in the still living and relatively healthy tissues for some distance around the sore.

These circumstances constitute a good *primâ facie* reason for regarding the parasite as the cause of the disease. On the other hand, there are many cases of dysentery in which the amœba cannot be found, cases, too, of relapsing dysentery with clinical characters such as the American authors referred to describe as belonging to amœbic dysentery. I have searched the stools in some such cases many times, but, though familiar with the appearance of the parasite, in a proportion of instances—just as has happened to other observers—have failed to find it, and this in well-marked dysenteries, acute, relapsing, and chronic. Moreover, as is well known, the amœba, or an amœba hitherto indistinguishable from amœba dysenteriæ, is found in perfectly healthy stools, in cases in which there is no reason whatever to suspect the existence of disease of the alimentary canal.

Gasser (*Arch. de Méd. Expérim. et d'Anat. Path.* No. 2, March, 1893), in material supplied by 153 cases of dysentery—principally soldiers from Oran—although he found amœba coli in 45 out of 109 acute cases, observed no relationship whatever between the number of amœbæ present in the stools and the severity of the disease. In 34 chronic cases he found the amœba in 13; and in 8 cases of chronic diarrhœa supervening on dysentery he found it in 5. In the stools of 20 healthy individuals from Oran he found the amœba in 4. He further states that he failed to find, or rather to recognise, the amœba in stained sections of dysenteric bowel. He concludes, therefore, against the amœba having anything more than an accidental relationship to the disease that, in place of the amœba

causing the dysentery, it is, if anything, the dysentery which causes or, rather, favours the amœba; in other words, the amœba finds in dysenteric discharges a favourable medium for multiplying in.

Celli and Fiocca (*Hygiene Institut.: Roman. Univ.*, Feb. 19, 1895) studied the parasitology of dysentery in material from 62 typical cases—some from Italy, some from Egypt. They, too, conclude that the amœba coli is not the direct cause of dysentery, and for the following reasons:—(*a*) Epidemic, endemic, and sporadic dysentery may occur without amœbæ in the stools. (*b*) Dysentery may be induced by the ingestion, or by the injection into the bowel, of dysenteric fæces which have been ascertained by microscopic examination to be quite free from amœbæ. (*c*) Amœbæ are very common in countries in which dysentery occurs, hence their frequency in the stools of dysenterics in these countries; they are there accidentally. They further point out that the amœba coli is not the only amœba to be found in the intestine; amœba guttula, diaphana, vermicularis, oblonga and reticularis, besides proteus, have all been found there. The amœba coli has attracted attention, they consider, principally on account of its movements and size; whereas the other amœbæ, with perhaps quite as good a claim to be considered pathogenetic, inasmuch as they can be detected only in specially-prepared cultures, elude the eye, even of the sharpest observer, in stools prepared in the ordinary way.

Bacterium coli commune.—Celli and Fiocca believe that dysentery is caused by the bacterium coli commune which, they assert, is always present in the stools in this disease. Generally non-pathogenetic, this bacterium, they and others believe, acquires in certain circumstances very virulent properties. They say that in the bowel it is often associated with a bacillus like that of typhoid, as well as with streptococci; and they assert that introduced by the mouth, or injected by the rectum, either or all of these particularly when in combination and in certain not

understood circumstances, either singly or in combination excite dysentery. They suppose that what they call the bacterium coli dysenteriæ is but a variety of the bacterium coli commune, a variety brought about in some way by the presence of the other bacteria mentioned; that in consequence of the presence of these other bacteria the bacterium coli commune acquires the power of secreting a specific toxin, which power it retains on being transferred from one human being to another. The toxin, they say, can be precipitated by alcohol from cultures, and has the property of giving rise to dysentery when administered by the mouth, the anus, or hypodermically.

These results require confirmation, more particularly as the writers experimented on the cat, an animal very subject to dysentery at all times and on the introduction of almost any irritant.

Streptococci.—Zancarol considers that dysentery and dysenteric liver abscess are caused by streptococci.

Significance of the concurrence of dysentery, liver abscess and amœba coli, in connection with absence of pus bacteria in the liver abscess.—The intimate connection of abscess of the liver with dysentery, and the presence of the amœba in the pus of a large proportion of liver abscesses, are now well-ascertained facts which, to my mind, constitute a powerful, though by no means a conclusive, argument for regarding the amœba as an ætiological element, if not the probable cause, in at least one form of dysentery. The fact that the amœba is found in liver pus proves that Councilman and Lafleur's statement about its presence in the tissues around the dysenteric ulcer is correct; for it is only by first passing into the tissues that such an organism could get into the portal circulation and so arrive at the liver.

There is yet another circumstance in connection with liver abscess which is not without a significance pointing in the same direction. In a large proportion of liver abscesses the usual pyogenetic bacteria are absent. This has been proved over and over again. Cultures made with such pus often remain sterile. It is a

very singular coincidence that it is just in those forms of suppurative hepatitis in which the usual pyogenetic organisms are absent that we find this other parasite present. Moreover, a liver abscess has no proper abscess wall. Liver pus is not like pus elsewhere; it contains proportionately very few pus corpuscles; but it contains much débris of the tissues, many blood cells, and much granular matter. As an abscess, it is altogether peculiar. A peculiar effect suggests a peculiar cause.

Anyone who has watched the movements of the amœba coli on the warm stage can readily understand how such an organism might break down and separate the anatomical elements of an organ like the liver, and so cause a softening—a cavity resembling an abscess. It feeds on the tissues, in fact, and to grow and multiply it must disintegrate their structures and consume their cells. I shall point out elsewhere that the amœba coli occurs much more frequently in liver abscess than is generally supposed; thereby strengthening the argument for regarding this parasite as being in causal relationship to liver abscess and, therefore, *pro tanto* to dysentery.

The germ of dysentery water-borne.—Notwithstanding the vast amount of speculation, and perhaps somewhat limited amount of work, expended in endeavouring to ascertain what the germ or germs of dysentery may be, it cannot be said that as yet we are even near the solution of the problem. One thing, however, is fairly well ascertained, and that is that these germs, whatever they may be, are often introduced by means of drinking water. The statistically ascertained improvement in the public health in respect to dysentery in such large towns as Calcutta and Madras following so closely on the introduction of improved water supplies; the improvement in the health of the British Navy following the introduction of regulations requiring that, in all places in which the water supply is not above suspicion, the drinking water served out to the men should be distilled;

constitute powerful testimony in favour of regarding dysentery as a water-borne disease. This conclusion receives additional support from the occurrence of epidemics of dysentery in the crews of ships which have watered at polluted sources; as well as by the occurrence of similar epidemics in large institutions in which, by some accident, surface water has leaked into the water supply. This, of course, does not exclude the possibility of other sources of infection, as by privies, and by vessels or instruments used by dysenterics; but the water theory probably covers the vast majority of dysentery epidemics, as well as of sporadic cases.

Predisposing and exciting causes. — It seems not improbable that, in conditions of sound health, the pathogenetic organisms of dysentery may exist in and pass through the alimentary canal without attacking the tissues and giving rise to the disease. So long as the mucous surface is sound and vigorous, it probably has the power of protecting itself against many such organisms. It is very probably the same in this respect with the dysentery germ or germs as with the cholera vibrio. It is probable that it is only on the establishment of some condition of lowered vitality, such as may be induced by catarrhal troubles, chill (a powerful excitant of dysentery), irritating food, bad food, constipation, malaria, scurvy, starvation, and so forth—all well-recognised exciting causes that the dysentery germ can overpower the natural protective agencies and light up the specific lesions. It is a well-known fact that it is in such circumstances that dysentery is most apt to declare itself. Hence the importance of avoiding these things in tropical climates, more especially in the presence of a bad water supply or of an epidemic. It seems probable that the well-known liability of lunatics to dysentery is associated with that lowering of the resistive powers which is so pronounced a feature in many forms of insanity.

Influence of age, sex, and occupation. —All ages

are subject to dysentery, children especially. Occupation has no special influence. Both sexes are liable. Pregnancy, miscarriage, and the puerperal state are grave complications.

Diagnosis. — Provided reasonable care be exercised, diagnosis, especially in acute cases, is usually easy. In chronic cases the question of hæmorrhoids, polypus, stricture, tubercle, malignant and specific disease, proctitis, abscess about the rectum, and tumour in the bowel, may require to be considered. Diagnosis must never be taken for granted. In every case stools must be inspected; and in every case in which there is any probability of rectal disease digital or specular examination must be made. In African cases the possibility of bilharzia disease of the rectum must be borne in mind, and a microscopical examination made of the urinary sediments and of the fæces with a view to the detection of any ova of bilharzia which may be present. In children especially, intussusception may occur independently, or as a complication, of dysentery; the possibility of this must not be overlooked. Chronic dysentery is often diagnosed chronic diarrhœa. This error will be avoided by careful inquiry into the early history of the case, the detection of mucus or of blood corpuscles in the stools, and the occurrence of tenesmus. Careful inquiry for any history there may be of occasional exacerbations, in which straining, blood and mucus in the stools, are more or less prominent features, will often lead to a correct diagnosis.

Treatment.—The treatment of dysentery requires much judgment and very careful supervision. In former days it was the fashion to bleed repeatedly and to large amount, and, at the same time, to administer large doses of calomel—amounting in the aggregate to ounces—and opium. It is not to be wondered at, therefore, that in those days the mortality was excessive.

Nowadays better and more rational methods

prevail. There is less confidence in drugs, more in the self-recuperating powers of the body. A most important part of our modern plans has for its object to afford the diseased organs favourable conditions for repair; not so much to endeavour to heal them, as to give them the opportunity of healing themselves.

If called on to treat a case of what appears to be dysentery, our first duty is to assure ourselves that diagnosis is correct. We must inspect the stools, and, until the case is quite recovered, we must inspect them daily. Their condition is the surest guide in the management of this disease. From them we can form a fairly accurate idea of what is going on in the bowel; and from them we can judge of the effects of diet and of drugs.

Importance of rest. — It is with an inflamed bowel as with an inflamed joint; the first and all-portant indication to fulfil is, after removing the causes of irritation, to place the part at rest. Could these two indications, the removal of the cause of irritation and the repose of the organ affected, be fulfilled thoroughly, cure would at once set in. Unfortunately, the affected surface being so inaccessible, we cannot always remove the irritant in the case of dysentery, nor can we place the parts involved at absolute rest. We can, however, partially meet these indications—quite sufficiently, as a rule, to insure recovery.

The diagnosis of dysentery established, the patient should at once be sent to bed. This in itself has a marked influence on the bowel. Repose must be as nearly complete as possible. The patient must not be allowed to get out of bed; when he has a call to stool he must use the bed-pan. To a certain extent this enforcement of rest is comparable to the placing of an inflamed leg in a splint and elevating it. It insures a certain amount of mechanical rest, and relieves the blood-vessels of the inflamed part of a certain amount of hydrostatic pressure.

Food in acute dysentery.—The indication of rest

we further endeavour to meet by stopping all solid food. Were it possible, it would be well to stop all food. This, of course, is impossible, and so we make a compromise between the therapeutical indication and physiological necessity, by reducing the diet to a minimum and selecting only such foods as, while possessing considerable nutritive value, yield but a small fæcal residue. The tongue is a fair index to the sort of food most likely to suit the case. When this organ is coated, indicating gastric catarrh, small quantities of thin chicken soup, egg albumin, thin barley or rice water, are better borne than milk; when the tongue is or has become clean, then milk, pure, diluted with barley- or rice-water, or peptonised, is the best diet. These foods should be taken in small quantities at a time, a little every hour. They must be given neither hot nor cold, as food when either too hot or too cold is more apt to excite peristalsis and to cause colic and straining.

Malaria and scorbutus.—If upon inquiry it is found that there is reason to suspect either a malarial or a scorbutic element in the case, treatment must be modified accordingly. Careful practitioners never forget to ascertain if these important complicating elements are present or not. If malaria be suspected, it would be well to make a careful microscopic examination of the blood for the plasmodium; if the parasite is found, then quinine must be freely administered either by the mouth or, if the bowels are very irritable, by hypodermic injection. The presence of scorbutus, of course, indicates fruit juices and fresh unboiled milk, in addition to the usual treatment for dysentery.

Drug treatment.—The patient has been sent to bed; a diet has been prescribed, malarial or scorbutic complications, should they be present, have been provided for; attention must then be directed to endeavour by one, or two, or three drugs to influence more directly the inflamed bowel.

The drugs which have proved of most service in

the treatment of dysentery are ipecacuanha, one or other of the aperient sulphates—either of magnesia or of soda—opium, and calomel. It is difficult to prognosticate in any given case whether ipecacuanha is likely to prove the more effective drug, or whether the sulphates or calomel will answer better. In every case one or the other ought to be exhibited at once; one failing after a fair trial, the other, unless manifestly contra-indicated, should get a chance.

Ipecacuanha.—In English practice ipecacuanha is generally the first to be tried. It must be given on an empty stomach. The best plan is to interdict all food for three hours; then to give fifteen or twenty drops of laudanum in a tablespoonful of water and, at the same time, to apply a mustard poultice to the epigastrium. About twenty minutes later, when the patient is coming under the influence of the laudanum, twenty to thirty—some give as much as sixty—grains of ipecacuanha in pill, bolus, keratine capsules, or in suspension in about half a wineglassful of water, are administered. With a view to prevent vomiting, the patient is directed to lie flat on his back—better without a pillow—and not to eat, drink, speak, nor move for at least three or four hours. Probably he will fall asleep. Should he feel nauseated, he must resist the desire to vomit as much as possible. With the same object in view, when saliva begins to collect in the mouth, as it is apt to do in such circumstances, it must not be swallowed; on a slight sign from the patient the nurse should remove the accumulating saliva with a handkerchief. If much saliva be swallowed, it is sure to provoke vomiting. In some instances these precautions suffice to avert emesis. Should, however, the ipecacuanha be brought up within an hour of its being swallowed, the dose had better be repeated so soon as the nausea has subsided, the same precautions against vomiting being observed.

After three or four hours, and when all feeling of nausea has subsided, small quantities of food may be

given, and frequent and fractional feeding persisted in for six or eight hours, or until the following day, when the dose of ipecacuanha must be repeated. As a rule, one or two such doses abort the dysentery, and the acute symptoms rapidly subside. It may be necessary to go on with the ipecacuanha once or twice a day for three or four days.

Aperient sulphates.—Should, however, this drug appear to be doing no good, sodium sulphate—which is less irritating than magnesium sulphate—may be tried (indeed, this may be preferred at the outset). These salts have the advantage over ipecacuanha of not causing nausea, and they are often quite as successful. They may be given in drachm doses in a little hot water every quarter of an hour until a purgative effect is produced, or they may be given in a large dose—half an ounce—to begin with, followed up by smaller doses if necessary. The purgative effect should be obtained once or twice daily, and for two or three days at least. The lessening of tenesmus and the production of copious, watery, feculent stools is the test of the successful action of the sulphates.

Calomel. — Should these means fail to control the disease, and should the bloody mucoid stools persist, and the griping and tenesmus continue, recourse may be had to calomel in combination with opium and ipecacuanha—a grain of each every five or six hours, the effect being watched and salivation avoided. Some give calomel from the outset as a routine treatment in dysentery, either in five-grain doses every six or eight hours, or in fractional doses every hour. This method is most in vogue in Germany, and is probably best suited for the croupous forms of the disease. In France the sulphates are most in vogue; while British physicians, relying on Indian experience, place most confidence in ipecacuanha.

Bismuth and opium.—As a result of either line of treatment, the dysenteric symptoms may subside rapidly —perhaps entirely. Sometimes, although the stools become fæcal, and the mucus and blood disappear,

a sort of diarrhœa remains. This generally quickly yields to a salicylate of bismuth (grs. x–xx) and morphia (gr. $\frac{1}{12}$) mixture.

Other drugs.—Simaruba (*ailanthus glandulosa*) sometimes succeeds where other measures have failed. It is a drug which, though nowadays neglected in Europe, is still much used in the East by so-called "dysentery doctors." It seems to be specially serviceable when the case has become subacute or chronic. To be effective, it requires to be given in much larger doses than is directed in the Pharmacopœias. One method of preparation I have seen employed is as follows:—Using an earthenware pot, boil half an ounce of simaruba in a pint and a half of water for three hours, and then strain it. Let the patient remain in bed and drink this decoction on an empty stomach every second morning for four times. Food must consist of milk and farinaceous stuffs. Another method is to boil an ounce of simaruba in twelve ounces of water until it is reduced to seven drachms; to this a drachm of spirit is added. This preparation, also, must be made in an earthenware or in an enamelled dish. For an adult this is a suitable dose; a child may take a fourth part. It should be taken every night for four nights.

Monsonia ovata.—Dr. John Maberly (*Lancet*, February 6th, 13th, 1897) reports very favourably on *monsonia ovata*—a South African plant—in dysentery. He uses a tincture of two and a half ounces of the dried plant to the pint of rectified spirit. It gave in his hands wonderful results, even in chronic cases and in acute cases which had resisted the ordinary remedies.

Cinnamon sometimes does good in chronic dysentery, as also *pomegranate*; either may be combined with simaruba.

I can offer no explanation of the action of any of these drugs in dysentery. We use them quite empirically. Ipecacuanha and simaruba really seem to have some sort of specific action on the disease or

on its cause, but in what way it is impossible to indicate. Strange to say, ipecacuanha, which has been found so serviceable in India, Africa, the Brazils, and elsewhere, has a very poor reputation as an antidysenteric in the United States (Osler); it has also signally failed in some English epidemics (Clouston); facts pointing to specific differences in the dysenteries of different countries.

Relief of pain. — During the attack the patient may suffer much from griping and tenesmus. These are generally relieved by hot fomentations, turpentine stupes, or by a hot bath. An excellent application is the Japanese hot-box, a small tin box containing a slowly-burning cartridge of powdered charcoal. Three or four of these hot boxes may be roughly sewn into a piece of flannel and laid on the abdomen. This application has the advantage of being very light, of not wetting the clothes, and of keeping warm for many hours. Tenesmus and dysuria are best relieved by morphia hypodermically; or by an enema of a wineglassful of thin starch containing forty or fifty drops of laudanum; or by suppositories of morphia and cocaine. Washing out the rectum with a pint of very hot water, with or without boracic acid, is sometimes effectual in removing for a time or, at all events, of mitigating the incessant desire to go to stool and to strain. Two drachms of bismuth with laudanum, thirty minims, and thin starch, two ounces, is also a good sedative enema (Davidson).

Treatment should be energetic and thorough at the outset of dysentery. Every effort must be made to prevent it from becoming chronic, as in this stage the disease is very difficult to treat successfully, and is prone to terminate in permanent invalidism.

Treatment of chronic dysentery. *Nitrate of silver injections.* — The most effective treatment of certain types of chronic dysentery is undoubtedly massive injections of large quantities of nitrate of silver solution of a strength of from half a grain to one grain to the ounce of distilled water. There is

a right and there is a wrong way of using this splendid remedy. If employed in the wrong way, it is useless, perhaps worse than useless. It must never be practised when acute symptoms are present. These must first be got rid of by ipecacuanha, by the sulphates, by calomel, and by rest and diet. The patient should be prepared for a week at least in this way. Then the bowel is to be cleared by a minute dose of castor oil, followed by a large enema of three or four pints of warm water to which two or three teaspoonfuls of carbonate of soda have been added. The whole of this injection having escaped, and when the bowel is quite empty, two to three pints of the nitrate of silver solution are thrown in by means of a long tube passed slowly and carefully into the bowel as far as it will go without kinking. It is better to fill the bowel by gravitation, using a funnel and tube, rather than by a syringe. The patient should be encouraged to retain the injection as long as he can, to lie flat on his belly, and to roll from side to side so as to secure that the injection comes in contact with every portion of the large intestine. If it seems to be doing good, this injection may be used every few days and kept up for some time. Improvement in suitable cases generally sets in at once. The nitrate must not be persevered with if it causes any marked irritation or increase of symptoms.

In the mild chronic dysenteries which are seen in Great Britain, and which originally had been contracted in the tropics, and also in the more acute relapses of tropical dysenteries, ipecacuanha should always be tried.

Other methods of treating chronic dysentery which succeed at times are the systematic washing out of the bowel daily with boracic water, with linseed infusion, with mangosteen rind decoctions, with weak alum water solutions, with tannin; systematic dosing with minute quantities of castor oil, with or without morphia; ten to twenty drops of turpentine three times a day; the daily consumption of some

preparation of fresh bael fruit; a course of Carlsbad, of Kissingen, or of Vichy water; a diet of grapes only, of milk only, or of beef only; cold water compresses to the abdomen.

Post-dysenteric constipation. — After the subsidence of a dysentery constipation and balling of the stools is by no means an uncommon event. This complication is best prevented, or met, by enemata of warm water to which a little salt has been added—a teaspoonful to the pint—or, if the bowel is very irritable, of linseed tea or of thin rice-water. An occasional dose of castor oil, half to one teaspoonful, once or twice a week or oftener, and kept up so long as the motions are not quite healthy, is an excellent routine practice; its action may be supplemented by a glycerine suppository. A course of Carlsbad waters or salts often gives excellent results.

Food and clothing.—In chronic dysentery much attention should be given to clothing and food. The former should be very warm. Dysenterics ought never to feel cold. Cold bathing is very dangerous for them; so are alcoholic drinks of all sorts. Food should be simple in the extreme. Beef, mutton, cheese, bread, coarse fruit or coarse vegetables, nuts, pickles, and such-like are, as a rule, not well borne. Fruit and fine well-cooked vegetables in moderation are necessary and often beneficial. In obstinate chronic dysentery it is often a good thing to change the diet from slops to solids, from a meagre to a more liberal one. Wonderful results are sometimes got from a sea voyage.

Hepatitis.—During the whole course of an attack of dysentery, and for months thereafter, the condition of the liver must receive the most careful attention. We may not be able to prevent abscess of this organ; but if pain and swelling seem to suggest it as threatening we can try, by means of saline aperients, ipecacuanha, rest, low diet, fomentations, dry cupping, and such-like measures, to avert what, to say the least, is a very grave complication.

Prophylaxis.—The prophylaxis of dysentery consists principally in securing a pure water supply, in avoiding unwholesome food, in temperance, in clothing warmly and avoiding chill, in correcting constipation and stopping diarrhœa.

CHAPTER XIX.

EPIDEMIC GANGRENOUS RECTITIS.

So far as known, this very fatal disease seems to be confined to the natives of the low-lying, hot, damp regions in the north of South America and, perhaps, to the natives of Fiji and other islands of the South Pacific. In Guiana it is known as "Caribi" or Indian sickness, in Venezuela as "Bicho" or "El Becho." It is said to be very contagious, and appears to be a form of rapidly-spreading phagedæna, which starts from the neighbourhood of the anus. Occasionally it may begin higher up—in the colon. In this case it is called the "high" form; in the other, the "low" or rectal form. Animals, as well as men, are attacked.

I am indebted to Dr. Ackers of Curaçoa, formerly of Venezuela, for the following information on the subject:—"I have only seen cases of the disease in animals, principally fowls, though also in dogs and calves; but I have been told by medical men, who themselves attended the cases, of its occurrence in children of the poorer classes. The disease commences by an itching in the anus, which produces an inclination to frequent defæcation. This stage continues for a few days, when a severe inflammation of the mucous membrane of the rectum sets in, giving rise to symptoms of acute dysentery. There are frequent stools of a mucous, bloody substance, accompanied sometimes by bile or excrement; at the same time, there is much straining, considerable elevation of temperature, anorexia, and great thirst. At this period, if the animal or child is not attended to, the above symptoms become more alarming; a constant flow of a slimy, fœtid, semi-liquid substance streaked with blood appears. Sometimes the discharge is of a

bright green colour, such as might be obtained by crushing tender stalks of grass. When this occurs the patients refuse all food, but the thirst is still intense. The affected animal remains standing in one place, with drooping head, as if overcome by fever and weakness. For a day or so it continues like this, until at last, unwilling to move, eat, or even drink, it suddenly dies in convulsions. Sometimes, however, this stage is not fatal, but is followed by prolapsus of the rectum, which is in a very inflamed state and ulcerated; rapidly gangrene sets in and is quickly fatal. The Venezuelan peasants state that this disease arises in children from chewing the green tender stalks of unripe maize, of which they are very fond on account of its sweetness. In children prolapsus of the rectum is very frequent; in fatal cases they may die, like the animals, in convulsions, though in children convulsions are not necessarily a fatal symptom. The treatment employed by the natives for animals consists in an enema of strong lemon juice, mixed with a weak dilution of white rum and water (aguardiente), two or three times a day; at the same time, the anus is freely dusted with wood ashes, some of which are also introduced into the rectum. A purgative of oil is generally administered also. In some cases I have known this treatment prove very successful. On the other hand, when the disease is too far advanced, or when the ulceration of the bowel appears at an early date, it seems to be of little or no avail. Another treatment employed, especially for children, consists in an enema of the juice obtained by crushing the stalks and leaves of *spigelia anthelmintica* (pasote). A decoction of the same herb is also given by the mouth three or four times a day. This decoction is very frequently administered by the peasants as an anthelmintic. In cases of children suffering from 'bicho,' one of the quarters of a lemon is roasted and introduced into the rectum as a suppository once or twice a day, and I have heard that it gives very satisfactory results."

CHAPTER XX.

HILL DIARRHŒA.

Definition.—A form of morning diarrhœa accompanied by flatulent dyspepsia and the passage of copious, liquid, pale, frothy stools. It occurs principally in Europeans on their visiting the hills after residing for some time in the hot lowlands of tropical countries.

Geographical and seasonal distribution.—Crombie, who gives an excellent account of this disease (*Ind. Med. Gaz.*, Dec. 1880; May, 1892), points out that a similar affection may show itself in the highlands of Europe as well as in those of India. It is said also to occur in corresponding circumstances in South Africa. There is no reason, therefore, to suppose that hill diarrhœa is special to India, although, owing to the large European population frequenting the hill sanitaria in that country, it has been particularly noticed there. An elevation of 6,000 feet or over, if combined with an atmosphere saturated with watery vapour, is particularly favourable to its development. In India it is found to begin and end with the rains, during which, in certain years and places, it is apt to assume almost epidemic characters. Thus, during the wet season of 1880 in Simla, an epidemic of hill diarrhœa affected from 50 to 75 per cent. of the population, three-fourths of the cases happening within a week of each other. In some years hill diarrhœa is less prevalent than in others; but at the proper season few of the various hill sanitaria of India are without examples.

Symptoms.—Without very obvious cause the patient, who in other respects may be in good health,

soon after arrival at a hill sanitarium becomes subject to a daily recurring diarrhœa, the looseness coming on regularly every morning some time between 3 and 5 a.m. The calls to stool are often sudden and imperative; the motions passed being remarkably copious, very watery in some instances, pasty in others, pale, frothy, and looking like recently stirred whitewash—so devoid are they of biliary colouring matter. Their passage is attended with little or no pain, often with a sense of relief. From one to half a dozen, or more, such stools may be voided in the morning before 11 a.m. After that hour, at all events in ordinary cases, the diarrhœa is in abeyance for the rest of the day, and the patient may then go about his duties or pleasures without fear of inconvenience.

The distinctive features of this form of diarrhœa are, therefore, the regularity of its recurrence every morning and its cessation after a certain hour in the forenoon; the absence of bile in the stools; and the attendant flatulence. The abdomen is sometimes blown out like a drum, the patient being conscious of unpleasant borborygmi, associated with a feeling as of some boiling or chemical operation proceeding in his inside. Occasionally cases are met with in which the stools are very pale, but in which there is no diarrhœa.

Under treatment, or spontaneously, or, according to Crombie, on acclimatisation occurring, after some days or weeks the diarrhœa may subside. In other instances it persists, in defiance of treatment, until the return of the patient to the warm plains, when it at once spontaneously subsides. Crombie instances a case in which the patient was regularly attacked with hill diarrhœa whenever he visited Simla—twelve occasions—recovery invariably taking place on his return to the plains. If the looseness is not only considerable, but also protracted, there necessarily ensue debility, wasting, and anæmia, and the disease may lapse into confirmed sprue—an affection having, apparently, close affinities with hill diarrhœa.

Ætiology and pathology.—It is difficult to say what may be the precise factors determining this disease. Low barometric pressure, associated with great elevation above the sea-level, may be a favouring circumstance. Damp seems to be indicated by the fact that the disease occurs principally during the rains. Chill after exposure to the high temperature of the plains has possibly an important share. Manifestly there is a suspension of the functions of the liver and, considering the dyspepsia and looseness, most probably of those of the pancreas and of the other glandular structures subserving digestion. Hill diarrhœa is certainly something more than an intestinal catarrh. As Crombie points out, it is more of the nature of dyspepsia. There are no adequate grounds for connecting it with either the water or the food supply. The question of micro-organisms has, apparently, not been studied.

Treatment.—The treatment recommended by Crombie, and endorsed by other medical men of experience in India, consists in a pure milk diet, rest, warm clothing, a teaspoonful of liquor hydrargyri perchloridi in water about fifteen minutes after food, and twelve grains of pepsine, or a corresponding quantity of lactopeptine or ingluvin, two hours after food. If, in spite of treatment, the disease persists, the patient must return to the low country.

CHAPTER XXI.

SPRUE (PSILOSIS).

Definition.—By the term "sprue" is understood a peculiar and very dangerous form of chronic catarrhal inflammation of the whole or part of the mucous membrane of the alimentary canal, generally associated with suppression of the chologenic function of the liver and, probably, of that of the other glandular organs subserving digestion. It is frequently met with in tropical countries, particularly in European residents. The same disease may develop for the first time in temperate climates; only, however, in individuals who have previously resided in the tropics or subtropics. Sprue is characterised by irregularly alternating periods of exacerbation and of comparative quiescence; by an inflamed, bare, and eroded condition of the mucous membrane of the tongue and mouth; by flatulent dyspepsia; by pale, copious and generally loose, frothy, fermenting stools; by wasting and anæmia; and by a tendency to relapse. It may occur as a primary disease, or it may supervene on other affections of the bowels. It is very slow in its progress; and, unless properly treated, tends to terminate in atrophy of the intestinal mucosa, which usually, sooner or later, proves fatal.

Nomenclature.—Sprue has been more or less recognised by writers on tropical medicine for many years. It has been called "tropical diarrhœa," "diarrhœa alba," "aphthæ tropicæ," "Ceylon sore mouth," "psilosis linguæ" (Thin), besides a variety of other names. The term "sprue" is an adaptation from the Dutch word "spruw" in use in Java, where the disease is very common.

Geographical distribution.—It is probable that sprue, although more common in certain warm countries than in others, is found throughout the greater part of the tropical and many parts of the subtropical world. It is especially common in South China, Manila, Cochin China, Java, the Straits Settlements, Ceylon, India, tropical Africa, and the West Indies (Hillary). Apparently it is most prevalent in those countries in which high temperature is combined with a moist atmosphere. It is common, however, in certain subtropical countries, as North China, and, occasionally, even in Japan; countries where, although the summer is hot and damp, the winter is dry and bracing.

Ætiology.—Prolonged residence in the endemic area is perhaps the most potent predisposing influence; cases, however, do occur in which the disease shows itself after a residence of one or two years only. Exhausting diseases, particularly those involving the alimentary canal, as dysentery, hill diarrhœa, morning diarrhœa, hæmorrhoids, and fistula, are apt to terminate in sprue. Frequent childbearing, miscarriages, uterine hæmorrhages, exhausting discharges, and prolonged lactation also predispose to the disease; so may syphilis, courses of mercury or of iodide of potassium, bad food, bad water, anxiety, chills, and so forth—in fact, any depressing influence, particularly if it is combined with intestinal irritation. Malaria does not seem to be specially responsible. At one time the anguillula stercoralis (p. 550), a parasite very common in the stools of cases of chronic intestinal flux, particularly in Cochin China, was put forward as the cause of the chronic entero-colitis (for the most part sprue) of that country. Subsequent investigations have disproved this. Like the anguillula, the amœba coli may be present in the stools in these cases; but, similarly, it is in no way responsible for the disease. Neither has any bacterium which can be regarded with any degree of certainty as special to sprue, been separated from the characteristic stools. In searching for the

fundamental cause of this affection, the latency which the disease occasionally exhibits, and the fact that the first symptoms may not appear until months or even years have elapsed since the patient quitted the tropics, must be kept in view.

Symptoms. — *Variability.* There is infinite variety in the combination and in the severity of the various symptoms of sprue, as well as in the rate of progress of the disease. In some instances it may be almost a subacute process running its course in a year or two, in others, again, it may drag on intermittingly for ten or fifteen years. Much depends in this respect on the circumstances, the character, the care, the treatment, and the intelligence of the patient.

General symptoms in a typical case. — In an ordinary fully developed case the patient — who is generally dark or muddy in complexion and much emaciated — complains of three principal symptoms: — soreness of the mouth, dyspeptic distension of the abdomen, looseness of the bowels; the last being particularly urgent during the morning and earlier part of the forenoon. The patient may also complain of feeling physically weak, of loss of memory, and of inability to take exercise or to apply his mind. His friends will probably volunteer the information that his temper is irritable and unreasonable.

Mouth lesions. If the mouth is examined, the soreness will be found to depend on a variety of lesions of the mucous membrane, which, though painful, seem to be of a very superficial character. These lesions vary considerably in intensity from day to day. During an exacerbation the tongue looks red and angry; superficial erosions, patches of congestion, and perhaps minute vesicles appear on its surface, particularly about the tip. Sometimes, from the folding consequent on swelling of the mucous membrane, the sides of the organ have the appearance of being fissured. The filiform papillæ cannot be made out, although here and there the fungiform papillæ may stand up, pink and swollen. If the

patient be made to turn up the tip of the tongue, very likely red patches of superficial erosion, sometimes covered with an aphthous-looking pellicle, may be seen on either side of the frænum. On everting the lips, similar patches and erosions are visible; and if the cheek be separated from the teeth the same may be seen on the buccal mucous membrane. Occasionally the palate is similarly affected; very often in this situation the mucous follicles are enlarged, shotty, and prominent. The gullet and uvula may also be raw and sore.

In consequence of the irritation caused by these superficial and exceedingly sensitive lesions, the mouth tends to fill with a watery saliva which may dribble from the corners. If the patient attempts to take any sapid food, strong wine, or anything but the very blandest diet, the pain and burning in the mouth are intolerable; so much so that, although perhaps ravenously hungry, he shirks eating. Not infrequently swallowing is accompanied and followed by a feeling of soreness and burning under the sternum; suggesting that the gullet, like the tongue, is also in an irritated, raw, and tender condition. During exacerbations of the disease the condition of the mouth becomes greatly aggravated. Although during the temporary and occasional improvements it becomes much less painful, even then salt, spices, strong wines, and all kinds of sapid food sting unpleasantly; and the tongue, particularly along its centre, is seen to be bare and polished as if brushed over with a coating of varnish. At all times the tongue is abnormally clean and devoid of fur; during the exacerbations it is swollen, but during the remissions, and when not inflamed, it is small, pointed, and, owing to the probably anæmic condition of the patient, yellowish like a piece of cartilage.

Dyspepsia.—Dyspepsia is usually much complained of, the feelings of weight, oppression, and gaseous distension after eating being sometimes excessive. Very likely the abdomen swells out like a drum,

and unpleasant borborygmi roll through the bowel. Occasionally, though not often, there may be vomiting, the vomiting sometimes being sudden and not always accompanied by feelings of nausea.

Diarrhœa.—The diarrhœa associated with sprue is of two kinds; one chronic and habitual, the other more acute and, in the early stages, evanescent. The former is characterised by one or more daily discharges of a copious, pale, greyish, pasty, fermenting, mawkish, evil-smelling material. The latter is of a watery character, also pale and fermenting, the dejecta perhaps containing undigested food. In these latter circumstances the diarrhœa usually brings with it considerable relief to the dyspeptic distension, at all events for a time. When the mouth is inflamed the diarrhœa is usually more active. The stools during periods of quiescence may be confined to one or two in the early morning or forenoon; during the later part of the day the patient is not disturbed. The stools, however, even in this quiescent phase, are always extraordinarily copious; patients remark their phenomenal abundance. They are passed almost, or altogether, without pain. Not infrequently during exacerbations there may be a tender excoriated condition of the anus, and sometimes, in women, a similar condition of the vagina. The stools in sprue are acid. (Thin.)

Types, history, course, and termination. Protopathic sprue.—There is a striking uniformity in the history of most cases of sprue. On inquiry, we shall probably learn that the patient has been suffering for months, or perhaps years, from irregularity of the bowels. This, we may be told, began soon after arrival in the tropics as a bilious morning diarrhœa. For a long time this morning diarrhœa went on, without interfering in any way with the general health. Later the mouth, now and again, became tender, little blisters or excoriations appearing for a day or two at a time about the tip of the tongue or inside the lips. These sore spots would come and

go. Perhaps, from time to time, exacerbations of the mouth symptoms would be associated with a little increase of diarrhœa. Gradually the stools lost their bilious character and became pale and frothy; dyspeptic symptoms, particularly distension after meals, now appeared. As time went on, these symptoms would recur more frequently and in a more pronounced form, following, almost inevitably, any little imprudence as regards food or exposure. The general condition now began to deteriorate; emaciation, languor, lassitude, and inability to get through the day's work satisfactorily, becoming more pronounced each summer until, finally, a condition of permanent invalidism was established. Should the disease continue to progress, the emaciation advances slowly but surely. Diarrhœa may be almost constant, and now no longer confined to the morning hours; the complexion becomes dark, sometimes very dark; the appetite, sometimes in abeyance, is more frequently ravenous; unusual indulgence in this respect being followed by increased discomfort, temporarily relieved by smart diarrhœa. Finally the patient is confined to the house, perhaps to bed. The feet now become œdematous, and the integuments hang like an ill-fitting garment, the details of the bony anatomy showing distinctly through the dry, scurfy, earthy skin. Finally, the patient dies in a semi-choleraic attack; or from inanition; or from some intercurrent disease. Such is the history of an ordinary, mismanaged case of sprue.

Sprue secondary to dysentery.—When the disease has supervened on dysentery, we shall learn that the motions characteristic of the original dysenteric attack gradually changed in character; from being scanty, mucoid, bloody, and accompanied with pain and tenesmus, they became diarrhœtic, pale, frothy, their discharge being followed by a feeling of relief rather than of pain. The mouth at the same time became sore, exhibiting the characters already described. Gradually a condition of

confirmed sprue was established, which ultimately, unless properly treated, will almost certainly prove fatal.

Sprue secondary to acute entero-colitis.—Another type of case commences as an acute entero-colitis with sudden and profuse colicky diarrhœa, vomiting perhaps, and a certain amount of fever. The acute symptoms do not subside completely, but gradually have the typical symptoms of sprue grafted on to those of an acute intestinal catarrh.

Incomplete sprue. (*a*) *Gastric cases.*—Occasionally we meet with cases of confirmed sprue in which, at first, the morbid process, judging from the existing clinical symptoms and subsequent history, is confined to a limited part of the alimentary canal. Thus we sometimes get sprue without diarrhœa, the principal symptoms being sore mouth, dyspeptic distension, pale but solid stools, and wasting.

(*b*) *Intestinal cases.*—On the other hand, we may get cases in which the mouth is not ulcerated, and in which there is little or no distension or dyspepsia, but in which the stools are liquid, copious, pale, and frothy. Sometimes a patient may have suffered at an earlier period, or on a former occasion, from the first type of the disease, who, later, acquires the diarrhœtic form ; and *vice versâ.*

(*c*) *Sprue without diarrhœa.*—It sometimes happens that under treatment the sore mouth, the dyspepsia, and the diarrhœa completely subside ; nevertheless the wasting continues, the stools remaining phenomenally copious—so much so that the patient may declare that more is passed than has been eaten. In this case wasting is progressive, and the patient gradually dies of inanition.

Intestinal atrophy consequent on sprue.—In certain instances, under treatment the symptoms proper to sprue subside ; but the patient's digestive and assimilative faculties are permanently impaired. Slight irregularities either in the quality or the amount of food, chill, fatigue, depressing emotions,

and other trifling causes suffice to bring on dyspepsia accompanied by flatulence and diarrhœa. These cases may linger for years; usually they improve during the summer in England, getting worse during the winter and spring, or during cold damp weather. Ultimately they die from general atrophy, diarrhœa, or some intercurrent disease.

Morbid anatomy.—*Post mortem* the tissues in sprue are abnormally dry; fat is almost completely absent; the muscles and the thoracic and the abdominal viscera are anæmic and wasted. With these exceptions, and certain important changes in the alimentary tract, so far as known there are no special lesions which are invariably associated with this disease. According to Bertrand and Fontan, occasionally certain changes are present in the pancreas—namely, fatty or granular degeneration of the cells, with softening of isolated acini and slight inflammatory infiltration of the connective tissue. These, however, are not constant, any more than are certain other and similar changes occasionally found in the liver and kidneys.

Lesions of the alimentary tract.—The principal and characteristic lesions are found in the alimentary tract. The bowel is thinned to such an extent as to be almost diaphanous. The serous coat is generally healthy, the muscular coat atrophied. The submucosa in places has undergone hypertrophic fibrous changes; and the mucous membrane from mouth to anus, either in patches or universally, is eroded and atrophied. The internal surface of the bowel is coated with a layer of dirty grey, tenacious mucus which conceals patches of congestion, of erosion, or even of ulceration, besides such evidences of similar antecedent disease as pigmented areas and thin-scarred, cicatricial patches. The villi and glands are eroded and in many places completely destroyed. Here and there minute spherical indurations, about the size of a pin's head and surrounded by a dark pigmented or congested areola, can be felt in the

mucous membrane. On cutting into these, they are found to be minute cyst-like dilatations of the follicles filled with a gummy muco-purulent material. Sections of the diseased bowel show under the microscope corresponding changes; such as varying degrees of erosion or ulceration of the surface of the mucous membrane; degenerations of villi, glands, and follicles; the small mucous cysts referred to; sometimes small abscesses; and, also, infiltration by leucocytes of the basement membrane and submucous layer; and, in the latter, fibro-cirrhotic changes. The mesenteric glands are generally large and pigmented, perhaps fibrotic. The ulceration lesions are usually most marked towards the end of the ileum and in the colon; but they may be present in greater or lesser degree universally, or in patches throughout the entire alimentary tract from mouth to anus.

Pathology.—In attempting an explanation of the phenomena of sprue, two features of the disease have to be considered—the catarrhal condition of the alimentary canal, and the absence of the normal colouring matter of the fæces. Possibly one of these is the consequence of the other; possibly the two conditions are concurrent but independent consequences of the same cause. What that cause may be is quite unknown. Whether the first pathological step originates in physiological exhaustion of the digestive functions, brought about by tropical conditions abnormal to the European constitution; or whether the disease depends upon a specific organism; or whether there is a combination of these, has still to be settled. In view of the occurrence of morning diarrhœa of dark bilious stools as a frequent first step in the development of sprue, hyperactivity of the liver might be assumed to be a first step in the development of the disease, an activity which in time ends in exhaustion of the chologenic functions of the gland. It might be further suggested that, concurrently with this hepatic disturbance, there is a similar initial hyperactivity of all the other glands

appertaining to digestion, a hyperactivity which also ends in a corresponding exhaustion. Chemical changes in the ingested food would then follow on these apeptic conditions, and ultimately, from the formation of acrid chemical bodies, lead to the chronic catarrhal changes found *post mortem.*

An analysis by Wynter Blyth of the stools in sprue resulted in ascertaining the presence of the ordinary elements of bile, notwithstanding their apparent absence so far as absence of colour would indicate. On the other hand, Bertrand and Fontan, in a similar analysis, failed completely to find bile acids. Until a decision is arrived at on this point it is useless to speculate further on the subject.

Micro-organisms, of course, abound in the fermenting stools of sprue; but hitherto no bacterium or protozoon which must be regarded as specific has been found in association with the disease.

Personally, I incline to regard sprue as an expression of exhaustion of the glandular structures subserving digestion, the result of over-stimulation by certain meteorological conditions which are found in tropical countries, and which are unsuited to the European constitution. The remarkable effect of physiological rest, as supplied by "the milk treatment," in curing sprue seems to support this hypothesis.

Diagnosis.—The condition of the tongue, the character of the stools, and the history are sufficiently distinctive, one would suppose, to render diagnosis an easy matter. Nevertheless, I have known of cases in which the disease has been diagnosed and treated as syphilis, the condition of the mouth being attributed to this disease, and the character of the stools and other symptoms being ignored.

Prognosis is good for recent cases, provided proper treatment is carried out. It is bad for patients over fifty, for long-standing cases, for careless and injudicious patients, and for those who cannot or will not take a pure milk diet.

Treatment.—*Importance of early and thorough*

treatment.—If treatment be undertaken sufficiently early in sprue, and be thoroughly and intelligently carried out, it is generally marvellously successful. Should, however, it be undertaken at too late a period, when the glands and the absorbing surface of the alimentary canal have been hopelessly destroyed, do what we will, the case is sure to end fatally. In prescribing a treatment, therefore, the first thing for the physician to do is to get his patient thoroughly convinced of the deadly nature of his complaint; for, unless he receives the hearty and complete co-operation of his patient, the physician must not expect to cure a well-established case. To be successful, treatment must be thorough, sustained, and prolonged, and all predisposing causes, as uterine or other discharges, syphilis, scurvy, and the like, must first be dealt with and, so far as possible, removed.

The milk cure.—By far the most successful treatment is what is known as the "milk cure." In carrying this out it is well to commence with a dose of some aperient—castor oil or pulvis rhei composita. Pending the action of the drug, all food, including milk, should be withheld. The patient should be sent to bed in order to economise strength and maintain an equable warm temperature of the skin. He should also be directed to clothe warmly, to encircle the abdomen with a broad flannel binder, to cover his arms and shoulders with a warm jacket, and to live in a warm room. When the purgative has acted the milk is begun. At first sixty ounces, at most, are allowed in the twenty-four hours, small quantities being given every hour. When the patient is very weak, the feeding must be continued during the night. The milk should not be drunk but sipped with a teaspoon, or taken through a straw or fine glass tube, or from an ordinary child's feeding bottle. As a rule, on this regimen, in the course of two or three days the patient's condition is very much improved. The stools have increased in consistency—are solid perhaps—the distension of the abdomen has

subsided, dyspeptic symptoms have vanished, and the mouth is much less tender and inflamed. The quantity of milk should now be increased at the rate of half a pint a day or every second day, until 100 ounces, or thereabouts, are taken in the twenty-four hours. It is well to keep at this quantity for ten days at least, when, everything going well, a gradual increase to six or seven pints may be sanctioned. Up to this point the patient should keep to bed; but when he has reached this quantity he may get up and, if he feels strong enough and the weather is mild, go out of doors. *For six weeks, dating from the time the stools become solid and the mouth free from irritation, no other food or drink whatever should be permitted.* A raw egg, if it is found to agree, may now be added to the milk; later, some artificial malted food; next, small quantities of well-boiled arrowroot, thin bread (stale) and butter, or other digestible form of starchy food; later still, chicken broth, a little fruit; and, by-and-by, fish and chicken may be gradually introduced.

Importance of prompt treatment of threatened relapses.—Should, however, the slightest sign of dyspepsia or flatulence, especially of diarrhœa, or of sore mouth show itself, then the extra food must be immediately suspended, a dose of compound rhubarb powder administered, and the patient be sent back to bed and placed once more at absolute rest and on a pure milk diet. In convalescents, no matter how long the acute symptoms have been in abeyance, this prompt recognition and treatment of threatened relapse should be rigorously observed. This is a rule of the utmost value and importance. Procrastination in treatment, under these conditions, is exceedingly dangerous. Promptitude in recognising and treating relapse not only saves time, but it may avert hopeless intestinal atrophy.

Symptoms persisting.—In commencing this treatment, if the patient after two or three days be found unable to digest and assimilate so much as

three pints of milk in the twenty-four hours, the daily allowance must be reduced by half a pint a day until thirty ounces or thereabouts only are taken. If now the motions become solid, the quantity of milk must be gradually increased by five or ten ounces a day, so that in the course of a few weeks the full allowance—six or seven pints—is consumed.

How to meet inadequate assimilation.—It sometimes happens that the quantity of milk can be raised to seventy or eighty ounces per diem, but no higher, further increase bringing on sore mouth, distension, and diarrhœa. In some of these cases the difficulty appears to depend not so much on digestion as on inability to absorb a large quantity of fluid. Occasionally, in such cases, one may succeed in getting the necessary amount of nutriment introduced by thickening the milk with condensed milk; or by slowly evaporating fresh cow's milk so as to reduce its bulk without diminishing the solids (Thin). The evaporation is best done in a vessel like a glue-pot, in which the milk is not boiled, but is surrounded by a jacket of boiling water; the milk during the process must be constantly stirred to prevent the formation of a scum. Or the milk diet may be supplemented by an adequate allowance of raw or underdone meat.

Other forms of giving milk.—Digestion is sometimes aided by peptonising the milk; or by mixing it with lime water or a little salt; or by aërating it in a soda water syphon (Goldsmith, *Brit. Med. Jour.*, July 1, 1893). Koumiss sometimes agrees for a time when ordinary milk fails, and, if necessary, should be tried. Similarly, white wine whey is occasionally digested when milk is not; it is often of great service, especially when an alcoholic stimulant is indicated.

Treatment with meat juice and underdone meat.—Occasionally, notwithstanding the utmost care and perseverance, symptoms persist or become aggravated under this system of treatment, and one is forced to conclude that milk does not suit the patient.

In my experience such cases are rare—very rare, but undoubtedly they do occur. In such circumstances raw meat juice will often prove an efficient substitute for milk. The juice of four or five pounds of fresh lean meat, and a little water to allay thirst, may be taken in small quantities at short intervals daily. After a time, when the stools are reduced in number and quantity, although perhaps not quite solid, scraped meat, or very much underdone meat, and by-and-by a little charred toast, a plain rusk or biscuit, and so forth, may be gradually added to the diet.

Meat and warm water diet.—Not infrequently, after the stools have become solid under a carefully regulated pure milk diet, it is found that any attempt to return to ordinary food, or to take anything beyond the most simple farinaceous dishes, is quickly followed by a recurrence of diarrhœa and the familiar flatulent dyspepsia. Such cases are sometimes successfully treated by a complete abandonment of milk, fish, and farinaceous stuffs for a time, and placing the patient on what is known as the "Salisbury cure." This is a diet consisting only of meat and warm water. Commencing with smaller quantities, in time the allowance of meat is gradually raised to about three pounds *per diem*, taken at equidistant intervals in three or four meals. The meat must be of good quality, free from fat, coarse fibre, and gristle; it may be prepared as mince, or in the form of steak or chop, not too much cooked. Warm water, amounting in all to four pints in the twenty-four hours, is drunk before going to bed and on rising in the morning, and also about two hours before meals —never at meals. This course must be persisted in for six weeks, when ordinary food is gradually attempted again.

Nutrient enemata or suppositories.—In all grave cases of sprue nutrient enemata or suppositories should be steadily administered every four or six hours. If tolerated they are most valuable aids to

nutrition. It is well, when using them, to wash out the rectum once a day with cold water.

These methods of treatment—milk and meat juice combined with rest—are the two most successful methods of treating sprue; should they fail, the chances are poor indeed.

When to send the patient to Europe.—When sprue develops in the tropics, if feasible, the patient should be sent to Europe as soon as possible. It is a mistake, however, to ship an invalid with his disease active on him, or if his end is manifestly not very far off. Diarrhœa should not be active when the patient is put on board ship. In every case provision, such as a cow or an abundant supply of sterilised milk, should be made for carrying on treatment during the voyage.

The clothing and general management.—Sprue patients who return to Europe ought to be especially careful in their clothing, and they ought to get out their warm clothes before the ship leaves the tropics. If their return is during the winter, they should arrange to remain in the South of Europe till at least late spring. Next to an unsuitable dietary, perhaps cold is the most prejudicial influence to which a sprue case can be exposed. A sprue patient ought never to feel cold; he ought always to wear thick flannels, thick stockings, and, when up and about, thick boots. In winter a chamois leather waistcoat, provided with sleeves, is of great service. His rooms ought to be warm. He ought never to be fatigued; he ought to go to bed early and rise late; in fact, he ought to do everything in his power to avoid irritating the bowel, to guard against chill, physiological depression, and the necessity for copious eating. During the summer England is suitable enough as a residence; but during the cold winter and spring months some milder, drier, and more sunny climate must be sought out.

Drugs in sprue.—Experience soon teaches one to distrust medicines in sprue. Occasionally a gentle

aperient or, if diarrhœa is watery and excessive, a few drops of laudanum are of service; but active drugging of all sorts is, as a rule, in the highest degree prejudicial. If the mouth is very painful, cocaine—five grains to the ounce—brushed on before eating will deaden sensibility and, for a time at all events, relieve suffering. Constipation must be carefully avoided, and a simple enema used if necessary.

I think it right to state that two methods of drug treatment seem, in some cases, to have been followed by good results. One, advocated by Dr. Begg, lately of Hankow, consists in the administration of repeated doses of yellow santonin. He recommends one or two doses of castor oil to commence with, and, thereafter, five grains of santonin in a teaspoonful of olive oil once or twice a day for a week, diet being at the same time attended to. The other method has gained for an irregular practitioner in Shanghai some reputation; it consists in the repeatedad ministration of purgatives alternately with or before the exhibition of large quantities—two teaspoonfuls at a time—of some form of carbonate of lime, believed to be powdered cuttlefish bone or powdered crabs' eyes. I have tried the santonin treatment without benefit to patients. I have also used cuttlefish bone; in one case with the result of permanently stopping the diarrhœa but not of arresting the progress of the disease. In this case, although diarrhœa was most effectively checked, yet massive solid stools continued to pass. After a few weeks the patient died from asthenia, notwithstanding a liberal diet which, apparently, was digested but not absorbed.

The sprue patient, if possible, ought not to return to the tropics. If compelled by circumstances to go back, he must exercise the utmost care with regard to his health, and avoid exposure, fatigue, cold bath, alcohol, and all excesses; take a minimum of, or avoid altogether, red meat; purge gently and go on absolute milk diet on the slightest sign of relapse.

CHAPTER XXII.

TROPICAL LIVER.

THE subject of liver disease is everywhere a difficult and complicated one. It is especially difficult in tropical countries; for not only is the resident there liable to all the forms found in temperate climates, but he is exposed, in addition, to various potent predisposing and exciting causes of liver disease not present, or only present in a very mild degree, in more temperate latitudes. These additional causes of liver disease, inseparable from the tropics, are heat, malaria, and especially dysentery. To these, too often, have to be added injudicious personal habits, a tendency to over-full and over-rich feeding, to over-stimulation by alcohol, and deficiency of muscular exercise.

The young European who finds himself in the tropics for the first time is surrounded very often by luxuries in the shape of food, wine, carriages, servants, luxuries to which he had not been accustomed perhaps in his home. At first the change, the excitement of novelty, and the high temperature act as stimulants to appetite, and the excessive loss of fluid by cutaneous transpiration creates a powerful thirst. Little wonder, therefore, that in such circumstances the youth, having the appetite and the opportunity of gratifying it, is apt to indulge in food and drink beyond safe physiological limits. He is made lazy by the heat; he cannot exercise during the day, and when evening comes he prefers lounging on the verandah or hanging about the club bar to walking, or riding, or games. Very likely he sits up late at night, drinking and smoking, so that in the

morning he is too sleepy to ride out or take any other form of exercise. And so it comes about, what with a surcharge of aliment and alcohol, and the diminished activity of lung metabolism and excretion incident to high temperature and muscular inactivity, that a very large and unusual amount of physiological work is thrown on the liver. With this large amount of work there is a corresponding hyperæmia. This may be considered the first stage of tropical liver—hyperæmia from functional activity; up to this point it is a purely physiological condition.

Pushed a step farther, however, this physiological hyperæmia passes into congestion with blood stasis and consequent diminished functional activity. Hyperæmia of a physiological character will be evidenced by increase of functional activity, and there will be a copious flow of bile, sometimes causing diarrhœa of a bilious character, particularly morning diarrhœa. But when the limits of physiological hyperæmia are passed, and congestion of a pathological character sets in, the consequent arrest of function will be evidenced by pale stools, perhaps diarrhœa of a pale, watery, frothy, fermenting character; in the latter case the diarrhœa doubtless depending, in part at least, on fermentative processes set up in the contents of an alimentary canal no longer kept relatively aseptic by an adequate supply of healthy bile. Other symptoms of this condition are headache, furred tongue, scanty, high-coloured, loaded urine, a feeling of weight or fulness, or even of pain in the region of the liver, and, probably, enlargement of the percussion area and other physical signs of enlargement of the organ. One step farther, and such a condition may pass into actual hepatitis attended with fever, smart pain in the liver, tenderness on percussion, and still more marked increase of the hepatic area.

A functionally very active hyperæmic organ is prone to inflammation even on slight cause. In the case of the hyperæmic liver a common cause is chill, such as may arise from a cold bath, a wetting, or

from lying uncovered on a warm night in a current of air. The experienced resident knows this very well, and is at great pains to guard against such an occurrence. He very likely wears what is known as a cholera belt, he sleeps, even on the warmest night, in flannel pyjamas, and with a thin blanket drawn over his abdomen; during the day he wears a woollen singlet and very likely serge or thin tweed clothes. He does not sit down in damp clothes, and he has a great respect for a shower of rain. Besides chill, there are other causes which may convert the hyperæmia into congestion or inflammation; a blow may operate in the same way, so may a surfeit of eating or drinking, so may exposure to the sun, so may an attack of malarial fever or of dysentery.

Treatment. Nature sometimes effects a cure in these cases of hepatic congestion by establishing a smart diarrhœa. In the treatment of such cases we cannot do better than to imitate Nature, and even to supplement her efforts. A few doses of the sulphates, in the shape of some kind of bitter water or of Carlsbad salts, generally give prompt relief. But if the subject of such attacks does not profit by experience and mend his ways, very likely his liver, in time, will become chronically hyperæmic and extremely liable to intercurrent attacks of congestion of a character more or less acute. The subjects of this type of "liver" ought to be most careful in their habits. They must not lie abed too long; they must not take cold baths, they must not take cold drinks, nor expose themselves to cold in any form; they must clothe warmly; and they must eschew alcohol in every shape. Animal food they must partake of but sparingly; and they should give the preference to fowl and fish over beef and mutton. Fruit and farinaceous food may be more freely partaken of, but over eating in every form must be avoided. Exercise should be taken at least twice a day, and, at least once in twenty four hours, the exercise should be of such a character as to provoke perspiration. A gallop on

horseback, a smart game of tennis or rackets, are excellent hepatic stimulants. Occasionally, once a week or not so often, particularly when a sense of fulness or aching in the right side seems to indicate that all is not right with the liver, a dose of Carlsbad salts or bitter water, preceded perhaps by a few grains of calomel, may avert more serious trouble.

When hyperæmia becomes chronic, when the patient is continually suffering with "liver," he should leave the tropics for a time. Nothing relieves these cases of chronic congestion so quickly or so effectively as a visit to Carlsbad and a thorough course of the waters there, and of the dietetic restrictions imposed in the Carlsbad cure. This should be followed up by country life in England and the active pursuit of country sports; the usual precautions in the shape of warm clothing, avoidance of cold baths, chills, alcohol, and high living being scrupulously observed and a weekly saline purge taken.

A serviceable imitation of the natural Carlsbad water may be made by dissolving fifty-three grains of the powdered salt in a pint of boiling water.* This may be divided into three equal portions, which are to be sipped as hot as possible, at intervals of twenty minutes, on an empty stomach, first thing in the morning. While taking the solution gentle exercise, as moving about the room, should be indulged in. Breakfast must not be taken till an hour after the last dose. If the bowels are not gently acted on an increased quantity of the salts should be taken. During the course, which should be persevered in for three weeks, the diet must be carefully regulated; butter, fat, nuts, fruits, pastry, preserves, tinned foods, cheese, salads, wines, spirits, and beer are to be avoided. Too much meat must not be taken; a small meat meal once a day must suffice. The quantity of food, too, should be restricted, and clothing, exercise, and bathing be carefully attended to. Much excellent

* A good substitute for Carlsbad salts consists of sod. sulph. 2 parts, sod. bicarb. 1 part, sod. chlorid. 1 part.

advice on the subject of the Carlsbad treatment will be found in Surgeon-Major Young's book, "The Carlsbad Treatment for Tropical Ailments," published by Thacker, Spink & Co., Calcutta.

During severe attacks of acute congestion, or of severe hepatitis attended with fever and much local distress, the patient must be kept in bed and placed on a very low diet of thin broths, barley water, or rice water, or milk and water. He should be purged freely and often with salines. A large hot poultice, two feet or more in length by one foot in breadth, should be laid over the region of the liver; such a poultice to be effective should pass from the centre of the back to well over the epigastrium. Dry cupping sometimes gives marked relief. Muriate of ammonia has a certain reputation in these cases; it should be prescribed in twenty-grain doses every six or eight hours. I have often used it, but I cannot vouch for its virtues; it does no harm.

When such a hepatitis is associated with dysentery, should it resist these milder measures, thirty to sixty grains of ipecac. often give marked relief. This dose should be repeated every twelve or twenty-four hours for two or three times. When the hepatitis is associated with malarial fever, full doses of quinine, in addition to the purging and to the other measures already mentioned, are indicated.

Whether hepatitis, unless associated with dysentery, ever passes on to suppuration is a moot point. Some say that it may; others resolutely deny that there is such a thing as "tropical abscess," unassociated with dysentery. This subject is discussed in the following chapter. Malarial hepatitis has already been considered (p. 92).

CHAPTER XXIII.

ABSCESS OF THE LIVER.

Definition.—A form of suppuration in the liver, occurring especially in warm climates, and principally in male Europeans and in association with dysentery.

Geographical distribution.—Abscess of the liver, of the type known as tropical abscess, is, for the most part, a disease of warm climates. Usually a sequel, or, it may be, a concomitant of dysentery, it is rare or altogether absent in countries where dysentery is also rare or absent. Its geographical distribution, therefore, is in the main regulated by that of dysentery. It has to be noted, however, that liver abscess is not a sequel or concomitant of the dysentery of all countries and at all times. Thus it is rare as an indigenous disease in temperate climates, even in those temperate climates in which dysentery is at times common enough. Again, in tropical climates the dysentery and liver abscess curves do not everywhere and at all times maintain a constant and definite relation to each other; for, even in hot countries, the dysentery of some places is more apt to be followed by liver abscess than is the dysentery of other places; and, even as regards dysentery in the same place, some epidemics are more apt to be associated with liver abscess than others are. Nevertheless, on the whole, it may be laid down as a fairly general law that in the tropics and sub-tropics the liver abscess curve follows in the main the dysentery curve; and that the geographical range of liver abscess in these climates is the same as that of dysentery.

In Great Britain the liver abscesses met with

occur most frequently in individuals who manifestly had contracted the disease in the tropics. As a disease of indigenous origin, notwithstanding the considerable amount of dysentery at times in some of the lunatic asylums and similar large public institutions in Great Britain, it is distinctly rare, though not so uncommon as is usually supposed. Of course this remark does not apply to those suppurations which are connected with ordinary pyæmia, with gall stones, hydatids, pylephlebitis, and the like; it applies only to dysenteric and, possibly, if there be such a disease, to idiopathic abscess. In northern and central Europe it is much the same in this respect as in Britain. The disease is more frequent in southern Europe—in Italy, Greece, the Balkan peninsula, and south Russia; it is said to be particularly common in Roumania. In eastern Asia, even outside the tropical belt, it is far from rare: thus it is not uncommon in Japan, and it is a very notable feature in the morbidity of Shanghai and the coast of South China. In Africa it is common enough; indeed, some of the best modern studies of the disease have been made in Egypt and in the Algerian province of Oran. In the western hemisphere there is a corresponding distribution; fairly common in the tropics, it becomes progressively rarer as we proceed north and south. It is apparently less common in the West Indies than in India and the East generally. In the southern hemisphere, although Australia seems to enjoy a practical immunity, the European in the neighbouring island of New Caledonia is said to be specially subject to this disease.

Ætiology.—*Relation to dysentery.* There can be no question as to the existence of an intimate relationship between dysentery and liver abscess. Numerous and well-authenticated statistics, as well as everyday experience attest this. In 3,680 dysentery autopsies made in various tropical countries, and collated by Woodward, 779 (21 per cent.) revealed abscesses of the liver. To quote recent Indian

experience: According to the Annual Report of the Sanitary Commissioner with the Government of India for 1894, out of 465 European soldiers who died from dysentery in India during the period 1888 94, 161 (35 per cent.) had, in addition to dysenteric lesions, abscess of the liver. Conversely, in Egypt, Kartulis, in an experience of over 500 cases of liver abscess, elicited a history of dysentery in from 55 to 60 per cent.; Zancarol, also in Egypt, in 444 cases, elicited a similar history in 59 per cent.; and Edwards and Waterman, in 699 collated cases, elicited a like history in 72·1 per cent. During the period 1870 95, of 45 cases of liver abscess treated at the Seamen's Hospital, Greenwich, and collated by Mr. Johnson Smith, *post mortem* evidence, or a distinct history, of dysentery was obtained in 38 (84·4 per cent.).

These figures are conclusive as to the existence of an intimate relationship between dysentery and liver abscess. There is good reason, however, for believing that, while they represent the truth, they do not represent the whole truth, and that the association is even more frequent than they indicate. As has been pointed out by Dr Neil Macleod and others, the occurrence of antecedent dysentery in cases of liver abscess is very often overlooked; for, without a *post-mortem* examination, it may be impossible to pronounce definitely on this point in every instance. It is also well known that extensive dysenteric ulceration may be present and yet give rise to no active subjective symptoms whatever. Moreover, it must be borne in mind that many patients suffering from liver abscess forget, or fail to mention, the occurrence of a previous dysenteric attack, and that they may mislead the physician by describing such an attack as "diarrhœa." Further, at *post-mortem* examinations, dysenteric lesions of a superficial and apparently trifling character are often either not sought for or they are overlooked. Consequently, although the evidence of antecedent dysentery may not be forthcoming in a proportion of cases of liver abscess, it

must not be concluded from this that there had been no dysentery.

In a masterly paper (*British Medical Journal*, October 26th, 1895) Macleod, after a very careful and critical analysis of certain figures bearing on this subject, concludes that dysentery is a factor in nearly every case of tropical liver abscess. In forty cases of the disease observed in Shanghai he had positive evidence of dysentery in all except one; and even in this case, as recovery ensued, there was no certainty that dysenteric lesions had not been present in it also. Perhaps Macleod's conclusions are somewhat too sweeping; I confess, however, that they are, in the main, in harmony with my own experience. Doubtless they apply to liver abscess as met with in Shanghai and, probably, in many other places. It is just possible, however, that what holds good for one place may not hold good for all places, and that Bombay, for example, may differ in this respect from Shanghai. In the Sanitary Commissioner's Report, above referred to, it is stated that in 2 (3 per cent.) instances only, out of 74 cases of liver abscess occurring in the Bombay Presidency in the period 1888–94, were there dysenteric associations. It is difficult to believe that, did it always exist, so important and evident a circumstance as dysentery had been overlooked 72 times in 74 cases. It is equally difficult to believe that the liver abscess of Bombay is associated with dysentery in only 3 per cent. of cases, whilst, according to the same authority, in the whole of India it is certainly so associated in at least 30 per cent. of the total cases. Manifestly, the statistical aspect of this important question requires re-study in the light of more careful clinical and *post-mortem* observation.

Another important point, yet to be definitely settled, is the exact relationship in point of time of the dysentery to the liver abscess. In the great majority of cases the dysentery antedates the abscess. But many clinicians have held that in some instances

the relationship is reversed; that in others the two diseases are from the commencement concurrent; whilst in others, again, hepatitis, presumably of a kind which may eventuate in abscess, alternates with active dysenteric symptoms. If the abscess antedate the dysentery, then the dysentery cannot be the cause of the abscess. On these grounds some pathologists have regarded liver abscess and dysentery as but different expressions of one morbid condition; reacting to some extent on each other, but not directly related the one to the other as cause and effect. Here, again, the latency as regards symptoms of some dysenteries has to be discounted in attempting to settle the question.

Race and sex.—Besides this matter of its relationship to dysentery, there are several well-ascertained facts to be reckoned with before we can arrive at sound views on the subject of the ætiology of liver abscess.

(1) Though common in Europeans in the tropics, liver abscess is rare among the natives. Thus, in the native army of India the proportion of deaths from liver abscess to the total mortality in 1894 was only 0·6 per cent., whereas in the European army it was 7·4 per cent. Man for man the relative liability of the European soldier and the native soldier was as 95·2 to 4·8.

(2) This disproportion is in spite of the fact that the native is more liable to dysentery than the European. Thus, in 1894, in the Indian army the admission rate among the native troops for dysentery was 43·8 per thousand, whereas in the European troops it was only 28·6; and in every hundred deaths in the native army 4·7 were from dysentery, against only 3·8 in the European army.

(3) European women in the tropics, though quite as subject to dysentery as European men, rarely suffer from liver abscess; children hardly ever.

(4) The rarity of liver abscess in temperate climates.

Predisposing conditions.—The foregoing considerations seem to indicate that for the production of liver abscess at least two things are necessary—a predisposing cause, and an exciting cause. Dysentery is certainly not always and alone both the exciting and predisposing cause. Were it so the native soldiers, and the European women and children, in India would suffer as frequently from liver abscess as do the European males there. Some additional factor evidently complicates the problem.

As liver abscess is developed principally in tropical climates and in European visitors there, and much more rarely in the native, it would seem that tropical conditions in those unaccustomed to them are in some way bound up with this predisposing element; and as liver abscess is rare in European women and children, it would seem that these conditions are in some way specially operative on European men. We have therefore grounds for concluding that, in addition to general tropical conditions, it must be the greater amount of exposure to which men, as compared with women and children, are subjected in the course of their business and amusements; or some other condition, especially that one which is relatively more common in men than in women and children—over-indulgence in stimulating food and alcoholic drinks—that constitutes this predisposing cause. Intemperate habits and exposure, doubtless, lead to a special liability in men to a hyperæmia and congestion of the liver tissue by which its resistive faculty to pathological influences is impaired. In these circumstances pathological influences, which in the healthier condition of the organ—such as we assume to exist more generally in natives and in European women and children would have been successfully overcome, gain the upper hand, and lead to suppurative disintegration of the organ. In support of this view we have the statement of Waring, that 65 per cent. of liver abscesses observed by him were in alcoholics; and it is also said, that when the native takes to

European habits in the matter of eating and drinking, his liability to liver abscess is greatly and proportionately enhanced.

I conclude, therefore, that in the vast majority of instances the exciting cause of liver abscess is dysentery; the predisposing cause hyperæmic, congestive, or degenerative conditions incidental to tropical life, supplemented by such things as exposure and unphysiological habits in eating and drinking.

Supplementary causes.—It is conceivable that in a highly predisposed liver exciting causes other than dysentery, such as a blow or sudden aggravation of chronic congestion by chill or excess, may suffice at times to determine suppuration. Liver abscess is most prone to develop at the commencement of the cold season. Further, one can conceive that in a hyperæmic liver struggling to resist dysenteric suppurative influences some third condition, such as the blow, chill, or surfeit referred to, may contribute to or determine the formation of abscess which, in their absence, might have been averted.

Briefly stated, the causes of liver abscess are, first, predisposing—hyperæmic and degenerative conditions of the liver; second, exciting—dysentery, or dysentery combined with chill, dietetic excess, or traumatism.

Influence of age and length of residence.—Liver abscess may occur at any age after childhood, but is most common between twenty and forty. It is most prone to show itself during the earlier years of residence in the tropics (40 per cent. in the first three years), although the older resident is by no means exempt.

Influence of malaria.—Malaria, by causing frequent attacks of hepatic congestion and by lowering the general vitality, may have some predisposing influence; but, as already pointed out, malarial hepatitis is essentially of a plastic and not of a suppurative nature. It is a common mistake to suppose that malaria causes the suppurative liver disease of the tropics; the two concur geographically, but are in no way ætiologically identical.

Organisms concerned.—The questions of the organisms concerned in liver abscess will be discussed in the section on pathology.

Symptoms.—There is great variety in the grouping of symptoms in liver abscess. The following is a common history.

The patient, after residing for some time in the tropics, during which he enjoyed good general health and lived freely, was attacked by dysentery. In due course he appeared to recover, and resumed work. Several weeks or months elapsed when, after a wetting, or some such incident, he began to feel out of sorts, to suffer from headache, foul tongue, want of appetite, irregularity of the bowels, disturbed nights, excessive and unaccountable languor, irritability of temper, and depression of spirits. About the same time he began to be conscious of a sense of weight and fulness in the right hypochondrium. Later, he became feverish, particularly towards evening, the oncoming of the febrile distress being sometimes preceded by a sense of chilliness. At times he had sharp stabbing pain in the right side in the region of the liver, perhaps a dry cough and, possibly, a gnawing, uncomfortable sensation or pain in the right shoulder. His friends observed that his face had become muddy and haggard. He was uneasy if he lay on his left side. The quotidian rise of temperature now became a regular feature, the thermometer every evening touching 102°—sometimes more, sometimes less—and sinking to near normal by morning. He now began to perspire profusely at night, and even during the day should he chance to fall asleep. He had to change his sleeping clothes once or even twice every night on account of the drenching sweats. On examination it is found that the patient is somewhat emaciated; his complexion thick and muddy; his pulse 80 to 100; his tongue is furred and yellowish; the palms of his hands and soles of his feet are cold and clammy. As he lies on his back it is obvious, on inspection, that the epigastrium is too full for one so

emaciated; and it is seen that the breathing is shallow and mainly thoracic. The right rectus muscle is found to be rigid. Considerable discomfort, if not pain, is elicited by attempts at palpation and percussion over the right hypochondrium. The liver dulness extends an inch too high, and an inch or more beyond the costal border in the nipple line; posteriorly, it rises to about the eighth rib in the line of the angle of the scapula. It is further observed that the line of dulness is arched along its upper border; and that it is not materially altered by changes of position, unless it be on standing, when the lower margin descends markedly in the epigastrium. Percussion below the right costal border, on deep inspiration, gives rise to much uneasiness or even to acute pain. Very likely one or two tender spots can be discovered on firm pressure being made with the finger tips in some of the lower right intercostal spaces, or below the right costal margin. The spleen is not enlarged. Auscultation may detect pleuritic friction somewhere over the base of the right lung, or peritoneal friction over the liver itself. The urine, free from albumin, is scanty, high-coloured, and deposits copious urates on cooling.

As the case progresses emaciation increases; hectic with drenching nocturnal sweats continues; the liver dulness and pain may further increase; or the general enlargement may somewhat subside, and percussion may reveal a pronounced local bulging, upwards or downwards. If the abscess which has now formed is not relieved by operation, after months of illness the patient may die worn out; or the abscess, which has now attained enormous dimensions, may burst into the right lung or pleura, or elsewhere, and be discharged, and either recovery or death from continued hectic and exhaustion, or from some intercurrent complication, ensue.

The great variety in the urgency of symptoms.—Although the foregoing is a fairly common history in liver abscess, there are many instances in which the

initial symptoms are much more urgent, and in which the disease progresses much more rapidly. In other instances subjective symptoms are almost entirely absent; or so subdued that the true nature of the case may be entirely misapprehended until the abscess bursts through the lung or bowel, or a fluctuating tumour appears in the neighbourhood of the liver; or, perhaps, not until after death, when the unsuspected abscess is discovered on the *post-mortem* table.

Fever.—In an acute sthenic case the initial inflammatory fever may run fairly high and persist for some time. Later, when it may be assumed that pus has formed, the fever becomes distinctly quotidian and intermittent in type, the morning temperatures being normal, or only slightly above normal, the evening rising to 101° or 102°, or a little over or under this. Sometimes evening temperatures of 103°, rarely of 104°, are registered. In the asthenic and insidious type, at first there may be short flashes of feverishness at more considerable intervals, to be followed later by a steadier fever of a hectic type, as in the suppurative stage of the sthenic cases. In either type there may be afebrile intervals of several days' duration; and in either there may also occur, concurrently with aggravations of the local conditions, spells of continued high temperature. Occasionally, though very rarely, liver abscess may be unattended by fever of any description whatever.

Rigors.—In the classical descriptions of liver abscess the occurrence of violent rigor is generally mentioned as a notable sign of the formation of pus. Undoubtedly such a rigor does at times signalise this event; but it is by no means constant, and its absence is no guarantee that abscess has not formed. Generally the evening rise of temperature is preceded by a sense of chilliness, sometimes by a more marked rigor simulating, in the regularity of its recurrences and in its severity, the rigor of a quotidian malarial fever.

Sweating, particularly nocturnal sweating, and

of a very profuse character, is an almost invariable accompaniment of liver abscess. The patient's clothes may be literally drenched with perspiration. Even during the day—particularly, as already mentioned, if he chance to fall asleep—the sweat may stand in beads upon the forehead and around the neck. This, like most of the other symptoms, may be temporarily absent, or, in a small proportion of cases, trifling.

The *complexion* is generally muddy, cachectic, and slightly icteric-looking; marked jaundice, however, is uncommon.

Wasting is generally decided and progressive.

Rheumatic-like pains and swelling of the hands and feet, such as occur in chronic septic affections, are sometimes to be noted. They usually disappear rapidly when the abscess bursts or is opened, and free drainage is established.

Pain of some description is rarely absent. In a few exceptional cases there is no pain; such a patient may declare that he does not know that he has a liver.

There are several types of pain—local and sympathetic—associated with liver abscess. Complaint is almost invariably made of a sense of fulness and of a sense of weight in the region of the liver, not infrequently referred to the infra-scapular region. Stabbing, stitch-like pain, increased by pressure, and especially by deep inspiration, coughing, and all sudden jarring movements, is very common, and probably indicates peri-hepatitis from proximity of the abscess to the surface of the organ. Percussion or firm palpation, especially if practised during deep inspiration and below the ribs in front, generally causes smart pain and decided shrinking, the rectus muscle starting up as if to protect the subjacent inflamed parts. Pain on swallowing, at the moment the bolus of food traverses the lower end of the œsophagus, was mentioned to me by a medical man, himself the subject of hepatic abscess, as being a

marked symptom in his own case. Pain on firm pressure with the finger tips in an intercostal space, and over a limited area, is a common and valuable localising sign. Among the sympathetic pains may be mentioned shooting pains radiating over the chest and down the right flank and hypochondrium.

Pain in the right shoulder.—This symptom is present in about one-sixth of the cases It may be persistent, or it may intermit; it may radiate to the side of the neck or to the region of the scapula, or down the arm; or it may be limited to the shoulder tip and clavicular region. In some instances it is of a dull, gnawing, aching character; in some it is more acute; and in some it may be represented by a burning sensation, as if the surface of the skin had been flayed by a blister. This symptom is a reflex transmitted from the hepatic terminals of the phrenic through the fourth cervical to the branches of the cervical and brachial plexuses.

Cough, of a dry, hacking character, doubtless also a reflex from irritation of the diaphragm, or from an inflamed condition of lung or pleura over the seat of abscess, is not uncommon. When the abscess discharges through the lung, cough is sometimes very severe, and may cause vomiting.

The *respiration* is generally shallow and proportionately rapid. This is partly symptomatic of the attendant fever; but it is often owing to the fact that fuller inspiration is attended with stitch. Sometimes the breathing is entirely thoracic, the lower part of the chest seeming to be fixed—especially the right side—and the diaphragm almost motionless.

The *decubitus* is usually dorsal or right dorsal, the body being somewhat bent towards the right side and the right leg perhaps slightly drawn up. When the patient stands, a stoop to the right may be noticeable. Lying on the left side generally causes pain from dragging on adhesions, or discomfort from the pressure of the enlarged liver on the heart and

stomach. Occasionally the decubitus is indifferent, or even on the left side.

The *digestive organs* are usually disturbed. The tongue is generally coated; vomiting may occur from time to time, arising either from pressure on the stomach by the swollen liver or as an expression of gastric catarrh; appetite, as a rule, is poor; flatulence may be troublesome, the bowels are confined or irregular, or there may be diarrhœa or dysentery. In the case of concurrent dysentery, it may be noted sometimes that the hepatic and dysenteric symptoms alternate in severity.

The *area of hepatic percussion dulness* is usually extended upwards and downwards, and sometimes horizontally. The extension may be general, especially in the earlier stages; later, careful outlining of the upper and lower boundaries may discover a limited and dome-like increase in one direction, most significant if upwards. The upper line of dulness is not, as a rule, horizontal, as in hydrothorax; almost invariably, on approaching the spine, it trends downwards more markedly than in hydrothorax or empyema. Variations in the extent of the dulness may take place from time to time, and sometimes very rapidly, depending on fluctuations—not in the size of the liver abscess, but on the varying and relative amounts of local and general hepatic congestion. One sometimes finds even a narrow hepatic dulness in the nipple line with a great increase in the axillary or scapular lines. In one case the lower border of the liver may be as low as the umbilicus, in another, especially in front, it may be well inside the costal margin. Diagnosis in the latter type of case is difficult, and depends rather on the nature of the fever, and on the history and general condition, than on local signs.

Splenic enlargement may be present even when there is no malarial complication. This is rare, however, and, in uncomplicated cases, is seldom great. I have seen splenic tumour closely simulated by abscess in the left lobe of the liver.

Varicosity of the epigastric and hæmorrhoidal veins —one or both of them—is sometimes discoverable.

Œdema of the feet and ascites are rare in the earlier stages; but the former is very usual towards the termination of long-standing cases.

Local œdema over one or more intercostal spaces, or more extensive and involving the whole or part of the hepatic area, is sometimes apparent. When limited it is a useful locating symptom.

Local bulging, if attended with fluctuation, indicates the presence of pus near the surface and the pointing of the abscess. Usually this, when it occurs, is in the epigastrium; but pus may burrow and find its way down the flank, or among the muscles of the abdominal wall, and open perhaps at a point remote from the abscess cavity in the liver.

Friction, both pleuritic and peritoneal, is sometimes to be made out, and is not without its value as a localising symptom.

Pneumonia, generally limited to the base of the right lung, and of a sub-acute and persistent character, indicates contiguity of the abscess to the diaphragm. It is especially common in those cases in which the abscess subsequently ruptures through the lung. This form of chronic pneumonia is a fruitful source of error in diagnosis.

Chronological relation of the hepatitis to the dysenteric attack.—This is most irregular and uncertain. In many cases of dysentery a concurrent hepatitis is manifest almost from the commencement of the attack; this hepatitis may not subside, but pass directly to abscess formation. Or the initial hepatitis and dysentery may both subside apparently, but the former may recur weeks, months, or even years afterwards when, perhaps, the attack of dysentery is almost forgotten. Or there may be no active hepatic symptoms with the dysentery, hepatitis supervening only long after all bowel trouble has passed away. In a few cases no dysenteric history can be elicited; it is seldom, however, as has already

been insisted on, that careful inquiry fails to bring out some story of previous bowel disturbance more or less urgent. In a few instances liver abscess of tropical origin does not declare itself until the patient has been several years resident in a temperate climate and quite outside the endemic area.

The *incidence of the symptoms* is equally variable. Some cases commence with marked sthenic fever, much local pain, great tenderness and hepatic enlargement, signs of suppuration as rigor, hectic, and local bulging, rapidly supervening. Others, again, commence so insidiously that the patient can hardly say when he first began to feel ill; perhaps there may be a history of slow deterioration of the general health during a year or longer before definite hepatic symptoms show themselves. The former type seems to be the more common in the young and robust newcomer to the tropics; the latter, in the more or less cachectic and old resident. Between these extremes there is endless variety.

Duration of the disease.—Liver abscess may run its course in three weeks. Generally it is an affair of several months. Sometimes it may run on for a year or even longer; particularly so if it burst through the lung and drainage be imperfect, in which event the cavity may keep on bursting and refilling at intervals for almost an indefinite period.

Terminations.—Apart from operative interference, liver abscess may terminate in various ways. It may end in spontaneous rupture leading to death or recovery. Death may also be brought about in other ways: by the severity of the local disease; by prolonged hectic and exhaustion; by concurrent dysentery, or by intercurrent disease as pneumonia, pulmonary abscess, empyema, peritonitis. Recovery may also ensue on the abscess becoming encysted, or, possibly, absorbed.

Rupture of the abscess.—Rendu in a series of 563 instances of abscess of the liver, compiled from various sources, gives an interesting table showing the direction of rupture in 159 (28 per cent.) of the cases which

causes of death are stated as follows :—Severity of the local disease, or through the associated dysentery, 125; bursting of the abscess into the peritoneal cavity, 12; into the pleura, 11; gangrene of abscess wall, 3; peritonitis, 3; pneumonia from effusion of liver pus into the lung, 3; rupture of adhesions, 2; pneumonia, 2; rupture into the pericardium, 1.

Morbid anatomy.—It may be inferred from the symptoms that in the early stages of suppurative hepatitis there is general congestion and enlargement of the liver; in some instances this condition may be more or less confined to one lobe or even part of a lobe. Later, as we know more especially from observations in cases that have died from the attendant dysentery, one or more greyish, ill-defined, anæmic, circular patches, half to one inch or thereabouts in diameter, in which the lobular structure of the gland cannot be made out, are formed. These grey spots are very evident on section of the organ. A drop or two of a reddish, gummy pus may be expressed from the necrotic patches—for such they are. Still later, the centres of the patches liquefy and distinct but ragged abscess cavities are formed. An abscess thus commenced extends partly by molecular breaking down, partly by more massive necrosis of portions of its wall; partly by the formation of additional foci of softening in the neighbourhood and subsequent breaking down of the intervening septa. The walls of such an abscess have a ragged and rotten appearance. Spherical on the whole, there may be one or more diverticula extending from the main cavity; or contiguous abscesses may break into each other and communicate by a sinus. Occasionally a thickened blood-vessel is met with stretching across the cavity. Though the pus and detritus lying on the abscess wall are viscid and adhesive, there is no notable exudation of lymph either lining the cavity, or in the still living liver tissue beyond. There is a peripheral zone of hyperæmia; beyond this zone the gland may appear normal or simply congested.

Number and size of abscesses.—Liver abscess may be single or multiple. If multiple, there may be two, three, or many abscesses. Zancarol's statistics, applying to 562 cases, give the proportion of single to multiple abscess cases as three of the former to two of the latter.

When single the abscess sometimes attains a great size. Frequently it is as large as a cocoanut or even larger; it has happened that the entire liver, with the exception of a narrow zone of hepatic tissue, has been converted into a huge abscess sac. When multiple the individual abscesses are generally smaller, ranging in size from a filbert to an orange.

As might be expected, from considerations of the relative size of the parts, abscess is more common in the right than in the left and smaller lobes. Roux gives the proportions in 639 cases as 70·85 per cent. right lobe, 3 per cent. left lobe, and 0·3 per cent. lobus spigelii.

Adhesions to surrounding organs are frequently, though not invariably, formed as the abscess approaches the surface of the liver. In this way the danger of intra-peritoneal extravasation is usually averted.

Pulmonary inflammation and abscess from escape of liver pus into the lungs are sometimes discovered *post-mortem*. Generally the pulmonary abscess communicates with the mother abscess in the liver by means of a small opening in the diaphragm.

Liver pus. — As already mentioned, the naked-eye appearance of liver pus is peculiar. When newly evacuated it is usually chocolate-coloured and streaked with, or mixed with larger or smaller clots or streaks of blood, and here and there with streaks of a clear mucoid material. It is so thick and viscid that it will hardly soak into the dressings, but lies on the surface of the gauze like treacle on bread; spreading out between the skin and the dressing, and finding its way past the edge of the latter rather than penetrating it. When quite fresh, here and there little islands

of yellowish, what may be described as, laudable pus may be made out in the brown mass. Sometimes it contains considerable pieces of necrotic tissue. Occasionally, from admixture of bile, the abscess contents are green-tinged. Liver purulage has always a peculiar mawkish odour; it is rarely offensive, unless the abscess lie near the colon, in which case it may have a fæcal odour. Under the microscope many blood corpuscles are discoverable, besides much broken-down liver tissue, large granular pigmented spherical cells, débris, oil globules, hæmatoidin crystals and, occasionally, Charcot-Leyden crystals, amœbæ, and the ordinary pyogenic bacteria.

Amœba coli and pyogenic organisms. According to my experience of tropical abscess of the liver seen in England, amœba coli can be detected in about half the cases. This is fairly in harmony with Kartulis's experience in Egypt, and that of others elsewhere. I have observed in a good many instances in which I have failed to detect the amœba in the aspirated liver pus, or in the pus which escaped at the time of operation, that the parasite appeared, often in great profusion, four or five days later in the discharge from the drainage-tube. I have seen them in these circumstances in strings of eight or ten, the string like arrangement suggesting that they had developed in some tube, such as a blood-vessel. The amœbæ persist in the discharge until the abscess has healed. It is justifiable to infer from the absence of amœbæ in the pus constituting what might be called the body of the abscess, and their appearance in the pus coming from the walls of the abscess a few days later, that the habitat of the parasite is not so much the pus occupying the general abscess cavity as that immediately in contact with the wall and the breaking down tissues themselves. This is an inference entirely in harmony with Councilman and Lafleur's demonstration of the parasite in the still living tissues around the abscess. In my experience the presence of the amœba does not affect prognosis unfavourably; Lafleur ("System of

Medicine," Allbutt, vol. ix., 1897) says it does, but I cannot agree with him, as I have many times seen amœbic liver abscess cases recover completely and rapidly after operation.

Other protozoa have been found in liver pus. Thus both Grimm and Berndt have found numerous active flagella therein. Some time ago, in the expectorated pus from a liver abscess discharging through the right lung, I found a ciliated infusorium resembling balantidium coli

In the pus of a large proportion of liver abscesses, both microscopic examination and culture may fail to detect the usual pyogenic micro-organisms. To harmonise this well-established fact with modern views on the cause and nature of the suppurative process, it has been suggested that, though in these sterile abscesses micro-organisms had originally been present, they had subsequently died out. This view receives a measure of support from the fact that in a proportion of instances there is no difficulty in demonstrating in the pus the ordinary pyogenic bacteria, and sometimes the bacterium coli communis. It by no means follows from this, however, that bacteria are a necessary factor for the production of all liver abscesses.

Encystment.—In rare instances the pus of liver abscess, instead of possessing the chocolate colour and viscid consistency described above, is yellow and creamy. This is particularly the case when the abscess becomes encysted—an occasional event. The walls of these encysted abscesses are thick, smooth, resistant, and fibrous. In time their contents become cheesey, and ultimately cretified; in the latter event the cyst shrivels up and contracts to a small size.

Pathology.—The pathology of liver abscess has been a fruitful source of speculation and controversy. Much confusion has crept into the question from attempts to separate, etiologically and pathologically, multiple from single liver abscess. The former is often called "pyæmic abscess" or "dysenteric abscess," and has been set down as being the peculiar

sequel of dysentery; the latter has been called and considered the "tropical abscess" *par excellence*, and regarded as idiopathic and entirely unconnected with dysentery.

As already pointed out, a careful examination of cases and statistics shows that both forms of abscess, single and multiple alike, are, in the vast majority of instances, clearly associated with dysentery. The dysenteric association, therefore, will not hold as a basis of classification and distinction. In their respective clinical histories, in their symptoms, in the characters of their walls and contents, in the frequent presence of amœba coli, single and multiple abscesses are practically identical. The only difference between them is a numerical one; also a circumstance quite inadequate to base a doctrine of specific distinction on.

The view which I incline to hold on this subject has already been partly indicated in the section on ætiology. There are two factors which are principally concerned in the production of liver abscess: (1) the predisposing — weakening of the resistive faculty of the liver by chronic congestion or tissue degeneration, and, perhaps, other subtle changes brought about by a combination of climatic, dietetic, and other tropical conditions; (2) the exciting—some micro-organism, streptococcus, staphylococcus, bacterium coli communis, amœba, or other parasite which, coming from the ulcerated dysenteric colon, or by way of the portal circulation, gains access to the liver and proliferates in the weakened tissues. In at least 90 per cent. of cases the pyogenic micro-organism is derived from dysenteric processes in the colon. Whether the resulting abscess be single or multiple is more or less a matter of accident. If the weakened liver is efficiently inoculated at one point only, there is only one abscess; if at many points, then there is multiple abscess. This is virtually, in a sense, Budd's theory expressed in modern terms.

An apparently weighty objection to this view is sometimes urged. Why, it is asked, if liver abscess

be the result of septic absorption from a dysenteric ulcer, is it not a common sequel of typhoidal or of tuberculous ulceration in the tropics? Macleod has met this objection very ingeniously and, I believe, to a certain extent, correctly. He points to the fact that typhoidal and tuberculous ulcerations are surface lesions unattended with abscess formation in the wall of the bowel. In their case there is free escape of the products and germs of ulceration; whereas in dysenteric lesions, in addition to the superficial ulceration, there is often what is really abscess formation with burrowing and retention of pus below the mucous membrane, and therefore great liability to entrance of micro-organisms into the radicles of the portal vein. Liver abscess, therefore, according to this view, is a pyæmic process. Often, however, it must be confessed, the dysentery preceding liver abscess appears, judging from the symptoms, to be of the catarrhal rather than of a more severe type.

To what extent amœba coli is concerned as an occasional, or even common, cause of liver abscess it is as yet impossible to state. But if we watch the movements of this animal on the warm stage; and if we reflect that it lives and wanders about in the same very active way among the structures forming the walls of the liver abscess, and even in what are comparatively sound tissues, preceding, as it were, the suppuration; and consider that it lives at the expense of these tissues, it is hard to resist the conclusion that the amœba operates as a disintegrating and irritating agency. Kartulis suggests that it may act merely as a carrier of pus-forming bacteria. Others maintain that it is a harmless epiphenomenon, incapable in any way of inducing pus-formation.

Calmette, in view of the frequency with which he and others have found liver abscess to be sterile, suggests that the exciting agency is of a chemical nature, some irritating liquefying body derived from the decomposition processes going on on the surface of the dysenteric ulcer.

Diagnosis. Of all the grave tropical diseases, none is so frequently overlooked as abscess of the liver. Acute sthenic cases are readily enough recognised; not so the insidious asthenic cases. The novice in tropical practice is some time in realising that grave disease of so important an organ as the liver may, for a long time, be unattended with urgent symptoms, whether local or constitutional, or both.

The most common mistakes in diagnosis are: (1) Failure to recognise the presence of disease of any description, even when an enormous abscess may occupy the liver. (2) Misinterpretation of the significance and nature of a basic pneumonia—a condition so often accompanying suppurative hepatitis. (3) Attributing the fever symptomatic of liver abscess to malaria. (4) Mistaking other diseases for abscess of the liver and *vice versâ*—for example, hepatitis of a non-suppurative nature, such as that attending malarial attacks, suppurative hepatitis before the formation of abscess; syphilitic disease of the liver—softening gummata, which are often attended with fever of a hectic type; pylephlebitis; suppurating hydatid; gall-stone and inflammation of the gall-bladder; subphrenic abscess; abscess of the abdominal or thoracic wall; pleurisy; encysted empyema; pyelitis of the right kidney; pernicious anæmia; leucocythæmia, scurvy and similar blood diseases associated with enlargement of the liver; ulcerative endocarditis. Any of these may be attended with fever of a hectic type, increased area of hepatic percussion dulness, and pain in or about the liver.

Many times a correct diagnosis can be arrived at only by repeated and careful study of the case in all its aspects. Golden rules in tropical practice are to think of hepatic abscess in all cases of progressive deterioration of health; and to suspect liver abscess in all obscure abdominal cases associated with evening rise of temperature, and this particularly if there be enlargement or pain in the liver and a history of dysentery — not necessarily recent dysentery. If

doubt exists, there should be no hesitation in having early recourse to the aspirator to clear up diagnosis.

As bearing on prognosis, apart from the risk from sudden rupture in some untoward direction, to overlook abscess of the liver is a much graver error than to mistake some other disease for liver abscess; for the chances of recovery from operation are proportionately prejudiced by every day's delay.

Low pneumonia of the right base in a tropical patient should always be regarded with suspicion; in most instances it means abscess of the subjacent liver.

Perhaps the most common error is to regard the hectic of liver abscess as attributable to malaria. The regularity with which the daily fever recurs, the daily chilliness or even rigor coming on about the same hour, the profuse sweating, and other circumstances so compatible with a diagnosis of malaria, all contribute to this mistake. So common is the error that Osler says he hardly ever meets with a case of liver abscess which has not been drenched with quinine. My experience is the same. I have seen medical men make this mistake, not only in their patients, but in their own persons. If carefully considered, there are several circumstances which should obviate so serious an error. (1) No uncomplicated ague resists quinine in full doses. (2) In malaria, if the liver be enlarged the spleen is still more so; the reverse is the case in liver abscess. (3) The plasmodium cannot be found in the blood in non-malarial hepatitis. (4) In liver abscess the fever is almost invariably an evening one; in malaria it most frequently comes on earlier in the day. (5) Quotidian periodicity, contrary to what is the case with tertian or quartan periodicity, is by no means pathognomonic of, nor peculiar to, malaria. (6) The almost invariable history of antecedent dysentery, or, at least, of bowel complaint in liver abscess.

To mistake other forms of suppuration for liver abscess is of no great moment, because in many of

the suppurative diseases just enumerated the treatment is the same as for liver abscess, and no bad result need be looked for if diagnosis is not quite accurate. A more serious error, however, is to overlook the presence of leucocythæmia, pernicious anæmia, or scurvy, and to proceed to aspirate an enlarged liver on the supposition that the symptoms arise from abscess. Fatal intra-peritoneal hæmorrhage from the puncture has been known to ensue in such circumstances. If any doubt exists on this point, a microscopic examination of the blood should be made before proceeding to explore.

A point to note in exploring is, that when the instrument enters the liver, an up-and-down pendulum-like movement will be communicated to the outer extremity of the needle in harmony with the rising and falling of the organ in respiration. If the needle does not exhibit this movement, its point may be in an abscess cavity but this abscess is not in the liver.

Treatment.—Hepatitis which has not proceeded to abscess formation should be treated, in the absence of dysentery, with free purging by the sulphates, massive hot poultices, low diet, and rest in bed. If there be much pain, relief may be afforded by either wet or dry cupping over the liver, or by leeches around the anus. Ammonium chloride, in twenty-grain doses three times a day, is usually prescribed. If dysentery be present, the case should be treated with full doses of ipecacuanha, repeated once or twice a day for two or three days, or by a cautious use of the purgative sulphates, and by poultices, rest, and low diet.

When the occurrence of rigor, or the development of hectic, or the appearance of local bulging, or the persistency of the fever and of the local symptoms, gives grounds for suspecting that abscess has formed, active medication must be suspended, a somewhat improved dietary prescribed, and measures taken without unnecessary delay to locate by means of the aspirator the position of the pus.

When he proceeds to use the aspirator, the surgeon must be prepared to open and drain the abscess if pus be discovered; once diagnosis is established, nothing is gained by delay. By proceeding to open the abscess at once the shock of a double operation is avoided, and only one administration of the anæsthetic is required.

To facilitate aspiration, as well as the subsequent operation if such should be found to be necessary, the patient ought invariably to be placed under an anæsthetic. Unless in very special and exceptional circumstances, it is a mistake to attempt exploration without this, for the surgeon ought to proceed with deliberation and to feel himself at liberty to make as many punctures as he may think necessary. A medium- or full-sized aspirator needle should be used, as, owing to the nature of the pus, it may not flow through a cannula of small bore.

If there are localising signs, such as a tender spot, a fixed pain, localised bulging, localised pneumonic crepitus, pleuritic or peritoneal friction, these should be taken as indicating, with some probability, the seat of the abscess and the most promising spot for the exploratory puncture. If none of these localising signs are present, then, considering the fact that the majority of liver abscesses are situated in the upper and back part of the right lobe, the needle should, in the first instance, be inserted in the axillary line in the eighth or ninth interspace, about an inch or an inch and a half from the costal margin and well below the limit of the pleura. The instrument should be carried in a direction inwards and slightly upwards and backwards, and, if found necessary, to its full extent. If pus be not struck, the needle must be slowly withdrawn, a good vacuum being maintained the while in case the abscess has been transfixed and the point of the needle lodged in the sound tissue beyond. No pus appearing in the aspirator, the remainder of the dull hepatic area must be systematically explored, both in front and behind, regard

run along the needle, and pushed through the intervening liver tissue and into the abscess. The aspirator cannula is now removed, and the blades of the forceps opened sufficiently, as it is being withdrawn, to make a wound in the liver large enough to admit the forefinger, which must now be inserted and moved about so as to enlarge the wound and to gain some idea as to the size and direction of the cavity of the abscess. A rubber drainage-tube, about as large as the finger, and provided with a flange, is cut to a suitable length, and carried by means of the forceps to the back of the abscess. The abscess is then allowed to empty itself. When pus no longer flows freely, a massive antiseptic dressing is applied and firmly secured by a broad binder or many-tailed bandage.

If after division of the abdominal wall no reliable adhesions be discovered between this and the liver, the capsule of the latter must be securely attached to the former by a double circle of stitches. The abscess is then to be opened, as above described, with sinus forceps. After stitching, some surgeons prefer before opening the abscess, first to stuff the wound in the abdominal wall with iodoform gauze, and to wait for a day or two for adhesions to form.

Should the abscess be struck through an intercostal space, and if the latter be not deemed sufficiently wide to admit of manipulation and free drainage, a couple of inches of rib had better be excised. The diaphragm may then be stitched to the thoracic wall or, better, to the skin as well, when the abscess may be opened with forceps. To stitch the capsule of the liver to the diaphragm is a somewhat difficult proceeding; but if there are no reliable adhesions it had better be attempted, especially if the opening is to be made through a part of the liver covered by peritoneum. If, by any chance, the pleura is opened during the operation pneumothorax will result, an unfortunate, but not necessarily a serious, contingency. In this case the hole in the pleura must be carefully stitched in such a way that

the pleural cavity is completely cut off before the diaphragm is divided and the abscess opened. Pus must not on any account be allowed to enter the pleural cavity; this, owing to the aspirating influence of inspiration, it would readily do if the smallest hole should remain patent. The young surgeon would do well to practise these operations on the dead body, and familiarise himself with the relations of the various structures they involve.

Some operators of experience completely ignore the absence of peritoneal adhesions, and, even in these circumstances, open the abscess without previous stitching of peritoneal surfaces. The risk and danger of escape of pus into the peritoneal cavity, they hold, is very small if free drainage to the outside is secured. Dr. Neil Macleod considers that, in the circumstances, stitches will not hold in the soft and inflamed liver tissue; he also considers that, in the event of the incision having to be made in the thoracic wall, removal of part of a rib is unnecessary. On account of the liability of the rubber drainage-tube to become nipped when the emptying sac causes a want of correspondence between the wound in the abdominal or thoracic wall and that in the liver, and, also, on account of facility of introduction during the subsequent dressings, this operator uses metal drainage-tubes of suitable lengths—four, three and a quarter, two and a half, and one and three-quarter inches—with an oval lumen of four-tenths by three-tenths of an inch. These tubes he introduces by means of a special guide (*Brit. Med. Jour.*, December 26th, 1891).

The author's method.—The following easy, rapid, and efficient method of operating on abscess of the liver I have frequently practised, and can recommend. The necessary apparatus (Fig. 29), which can be made by native workmen, consists of a large trocar and cannula (*a*), four to five inches long, by three-eighths of an inch in diameter; a steel stilette (*b*) at least fourteen inches in length; two metal buttons (*c*, *d*) $\frac{1}{4}$ inch at their

greatest diameter, with long (half-inch), hollow, roughened necks into which the ends of the stilette fit loosely; six inches of half-inch stout drainage tubing (*e*). While the ends of the drainage tubing are held and well stretched by an assistant, they are firmly lashed to the stem of the buttons, over the ends of the shorter (*d*) of which, for additional security, the

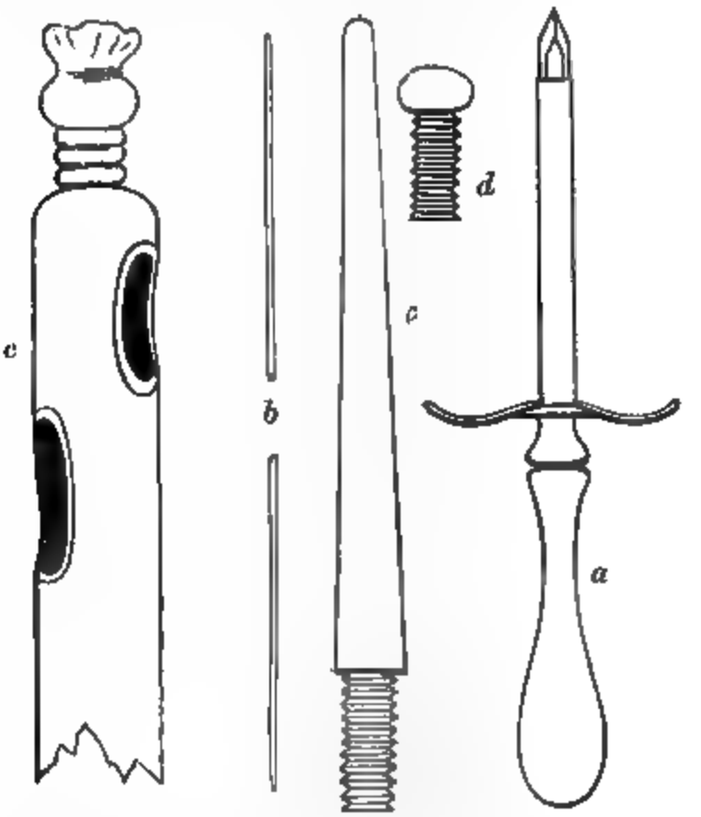

Fig. 29. – Apparatus for operation for Abscess of the Liver. *a* and *b* reduced.

tubing is also tied (*e*). Two large holes, to provide for free drainage, are then cut close to one end of the drainage tube. The tube is then mounted on the stilette by inserting one end of the latter through one of the drainage holes and lodging it in the hollow neck of the distal button (*d*, *e*), and thereafter so stretching the rubber that the other end of the stilette can be inserted into the neck of the other button (*c*). When thus stretched, the drainage-tube should be capable of

passing easily through the cannula. The apparatus being thus prepared and rendered thoroughly aseptic by soaking in carbolic lotion, and the position and depth of the abscess having been carefully ascertained by means of the aspirator and noted, the aspirator is withdrawn and an incision about an inch in length made with a scalpel through the skin at the site of the puncture The trocar and cannula are then thrust into the abscess and the trocar is withdrawn. After allowing a small quantity of pus to escape, so as to relieve any tension that may be present in the abscess sac, the stretched drainage-tube, perforated end first, is slipped into the cannula and carried to the back of the abscess. Holding the stretched drainage-tube firmly, and maintaining it carefully in contact with the back of the abscess with one hand, the cannula is withdrawn with the other. Still grasping the drainage-tube firmly, the button on the free end of the apparatus is slipped off the stilette, the end of which is made to perforate the drainage-tube close to the button. This it readily does, and the drainage-tube is allowed slowly to resile towards the fixed end, still held in contact with the back of the abscess. When the drainage-tube has completely contracted, the stilette is withdrawn. The drainage-tube is now transfixed with a safety pin inserted close to the skin, and the superfluous tubing cut off. Pus flows freely from the tube, which now firmly plugs the wound in the abdominal wall and liver, and bridges the peritoneal cavity. When the abscess has nearly emptied itself the usual antiseptic dressing is applied. In operating through the thoracic wall, if deemed desirable, part of a rib may be excised before the trocar is introduced.

I claim for this operation that it is easily done, and that it may be undertaken by the merest tyro in surgery and in the absence of skilled assistance; that there is no risk from bleeding; that, the peritoneum being bridged across by the drainage-tube which is securely grasped by the liver tissue, there is no risk

of escape of pus into the peritoneal cavity; that in a very short time lymph is effused around the tube, giving additional security when, after a time, the tube has become loose; that, if deemed necessary, a larger drainage-tube, by stretching it on the stilette in the same way as described, can be substituted for the half-inch tube; that an abscess deep in the liver can be as readily opened, and with as little risk, as one lying near the surface; that the shock is much less than in the cutting and tearing operation; that there is no risk of pneumothorax should the pleural cavity be traversed; and that the drainage obtained is equal to that secured by any other method of operating. Several of my surgical friends have adopted this method of operating, and have expressed great satisfaction with the ease with which it is performed, and with the results.

Other operations. — Some Continental surgeons recommend extensive incision of the liver, using a Paquelin's knife with the view of minimising bleeding. Zancarol, for example, advises that the hepatic and integumental incisions should extend the whole breadth of the abscess cavity, which he mops out, and stuffs with iodoform gauze. Certain French surgeons recommend scraping the abscess cavity; most of them practise irrigation with some antiseptic fluid. These methods do not find favour with English or Indian surgeons.

The method of opening the abscess by caustics, formerly much in vogue, is now abandoned; equally so another method, also formerly employed—namely, that of leaving a rigid trocar in the wound.

Treatment after operation.—For the first few days after a liver abscess has been opened the discharge is considerable, and the dressing may have to be changed frequently. Very soon, however, should the case do well, the discharge rapidly diminishes, and the dressing requires renewal only every other day or every three or four days. During the first week the drainage-tube, provided it be acting efficiently, should not be

disturbed, more particularly as it may be difficult to replace. Later, it may be removed and cleaned, and when discharge has practically ceased, cautiously shortened; it is a great mistake, however, to begin shortening the tube before it is being pushed out, or so long as there is any appreciable discharge. If there is the slightest indication, such as rise of temperature, that pus is being retained, the sinus must be dilated with forceps and finger, and a full-sized drainage-tube introduced as far as it will go If this does not suffice, a counter opening may have to be made. Delay in remedying imperfect drainage is a serious error.

Should an abscess on being opened be found to be septic, or should it become so, it must be flushed out daily, or twice a day, with a weak non mercurial antiseptic, and a counter opening made if necessary.

After liver abscess has been opened and is draining well, temperature rapidly falls and, in a few days or almost at once, becomes normal. Should fever persist, it is to be inferred either that the drainage is inefficient, or that there are more abscesses in the liver, or that there is some complication. If it be deemed that there is another abscess, this should be sought for with the aspirator, and, if found, opened and drained. I have seen a patient recover after three abscesses had been so treated.

Treatment of abscess discharging through the lung.—In the case of abscess discharging through the lung, and not progressing favourably, the question of obtaining by surgical means more efficient drainage must be considered. There are two possibilities which render interference desirable. (*a*) Continued discharge of pus and blood, with or without attendant hectic; a condition which, if it persists, in all probability will in the end kill the patient. (*b*) Not infrequently prolonged discharge through the lung may induce fibrotic changes in that organ, or may give rise to pneumonia, or to abscess of the lung with all its attendant dangers.

In these circumstances it is sometimes difficult to arrive at a decision as to whether an attempt should be made to open and drain the abscess, or to leave it alone. A large proportion of the cases recover, but at least an equally large number die. Of the latter, by timely surgical interference, a proportion may certainly be saved.

In all cases of abscess discharging through the lung a careful register should be kept of three things —body temperature, daily amount and character of expectoration, and, once a week, the weight of the patient. If temperature keeps up, if the amount of pus continues the same or increases, or if the patient continues to lose weight, an attempt should be made at all risks to reach and drain the abscess from the outside. If temperature keeps normal, if pus gradually or intermittingly decreases, and if the body-weight be maintained or increases, operation is unnecessary, or, at all events, should be deferred.

In exploring the liver in such cases, it must be borne in mind that most likely the abscess cavity is collapsed, and that the sides of the abscess are in contact. Such an abscess is not likely to be discovered unless the needle be thrust in to its full extent, and, whilst a good vacuum is being maintained in the aspirator, slowly withdrawn. If by good fortune the abscess has been traversed, then, when the end of the needle crosses the cavity, a small amount of pus will be seen to flow. Great care must now be exercised to keep the needle in position so as to serve as a guide in opening the abscess. Recovery has been known to follow the introduction of a drainage-tube in the presumed direction of such an abscess, even although the abscess cavity was not entered, much less drained by the tube.

Treatment of abscess rupturing into a serous cavity.—When there is evidence that an abscess of the liver has ruptured into the peritoneum, into the pleura, or into the pericardium, the particular serous cavity involved must be opened at once and treated

on general surgical principles; otherwise, the patient will almost surely die. In the circumstances the surgeon will be justified in assuming great risks.

The *prognosis in early operations* on single abscess of the liver, provided there is no dysentery or other complication, is good. In multiple abscess, or in single abscess if there is active dysentery or other serious complication, prognosis is bad. In multiple abscess, if there are more than two or three abscesses it is necessarily hopeless.

The *question of return to the tropics* after recovery from liver abscess frequently crops up. If feasible, and if the patient has not to make too great a sacrifice, he ought to remain in a temperate and healthy climate. There are many instances, however, of individuals who have enjoyed permanent good health in the tropics after recovery from liver abscess.

CHAPTER XXIV.

INFANTILE BILIARY CIRRHOSIS.

WITHIN the last fifteen or sixteen years, a peculiar disease of the liver has been noticed in children in Calcutta and, to a less extent, in other large towns of India. It is found to be more prevalent in Hindoo than in Mahomedan children. Thus in Calcutta, from 1891 to 1893 inclusive, infantile biliary cirrhosis, the name given to this disease, caused 1,748 deaths. Although the Hindoo and Mahomedan populations of that city are about equal, yet as many as 1,616 of the deaths occurred in Hindoos, whilst only 80 occurred among Mahomedans, the balance of the mortality being among the Eurasians and other races. The disease occurs principally in children under one year, rarely attacking those over three years. As a rule, it commences during dentition, or about the seventh or eighth month, running a fatal course in from three to eight months. In rare cases it may commence within a few days of birth. Instead of lasting several months, its progress may be much more rapid, and terminate in death in from two to three weeks.

The cause of infantile biliary cirrhosis is quite unknown. Neither alcohol, syphilis, nor malaria has anything to do with it. The children of the well-to-do are relatively more frequently attacked than those of the poor. It has also been observed that it tends to run in families, child after child of the same parents succumbing within a year or two of birth. In 400 cases, Ghose had only six recoveries, and in some of these recoveries the diagnosis was doubtful.

Symptoms.—Commencing insidiously, the cha-

racteristic initial enlargement of the liver may have made considerable progress before the disease is suspected. Nausea, occasional vomiting, sallowness, feverishness, constipation, anorexia, irritability of temper, thirst, and languor call attention to the child's condition. On examination, the liver is found to be enormously enlarged, extending perhaps to the umbilicus or even lower. The surface of the organ is smooth; the edge, at first rounded and prominent, as the liver begins to contract becomes sharp and distinct and can be readily grasped between the fingers, the swollen organ feeling hard and resistant. Fever of a low type sets in; the sallowness deepens into profound jaundice; the stools are pale, the urine is dark; and there may be ascites, with puffiness of the feet and hands. Sooner or later, death from cholæmia ensues.

Pathological anatomy and pathology.—Surgeon-Major Gibbons, who has given an elaborate and most careful account of the pathological anatomy of this disease, concludes that it is a peculiar form of biliary cirrhosis, the consequence of the action on the liver cells of some irritant of gastric origin, which leads to degeneration of the cells in the first instance, with subsequent increase of intercellular connective tissue and, later, of the portal sheaths. The formation of new bile ducts between the hepatic cells, which is a well-marked feature, he regards as evidence of a natural curative effort having for its object a regeneration of the liver cells.

Treatment.—Hitherto, in this disease, treatment has been of little avail. There is some ground, however, for thinking that early removal from the endemic locality, and a complete change of wet-nurse and food might have a beneficial effect. (*Trans. First Calcutta Med. Cong.*)

CHAPTER XXV.

PONOS.

UNDER the name "Ponos" Karamitsas (*Gaz. des Hôpit.*, 1880) and Stephanos (*Gaz. Heb. de Méd.*, 1881) have described a peculiar disease endemic in the islands of Spezzia and Hydra in the Grecian Archipelago. Ponos, in a sense, is analogous to the infantile biliary cirrhosis of Indian cities. Like the latter, it is confined to very young children, it is endemic in particular districts, tends to run in particular families, to pursue a more or less chronic course, and is invariably associated with disease of an abdominal viscus—in this case the spleen. Though not invariably so, it is usually fatal.

Symptoms.—Commencing somewhat suddenly and, commonly, during the first year of life, the earliest symptoms to attract the attention of the parents are languor and a pallor which rapidly acquires a sallow tint. Fever of an irregular character sets in; the spleen enlarges; prostration is very marked; and, it is said, the urine exhales a peculiarly disagreeable odour. Emaciation becomes progressive. Although the digestion is enfeebled and constipation is nearly always present at first, the appetite is fairly preserved and may be perverted or excessive. The spleen gradually attains a great size, and is tender—hence the name, "ponos" (pain). The associated fever is of an irregular character, tending to become remittent, the thermometer rising during the exacerbations to 39° or 40° Cent.; towards the end it acquires hectic characters. Complications in the form of bronchitis, pneumonia, diarrhœa, dysentery, peritonitis, or meningitis may show themselves. When

the disease has been established for some time œdema and ascites may occur, and there may be hæmorrhages in or from various organs, especially the gums. In certain cases boils, and even patches of superficial gangrene, are met with. The progress of the disease is very variable; it may last from one or two months to one or two years.

Pathological anatomy and pathology.—Of these nothing is known further than that ponos exhibits none of the characteristic lesions of tuberculosis, of leukæmia, or of malaria. Its cause is quite unknown. It has been remarked, however, that it is prone to occur in the children of those who have themselves suffered in infancy in the same way. It is said that in the case of the disease attacking the child of a tuberculous mother, recovery will very promptly set in if the child be supplied with a healthy wet-nurse. It has been suggested that ponos is an expression of malaria, but the *post-mortem* evidences are altogether against this supposition; moreover, malaria is said to be unknown in the two islands in which this peculiar disease is endemic. The tendency to bleeding from the gums, cutaneous ecchymoses, and liability to hæmorrhages suggest a scorbutic element. Ponos affects the children of rich and poor alike, and those living in good as well as those living in dirty, unhygienic houses.

Treatment.—No specific is known. Quinine, tonics, fruit juices, careful management of the food, and early change of residence would seem to be indicated.

SECTION IV.—INFECTIVE GRANULOMATOUS DISEASES.

CHAPTER XXVI.

LEPROSY.

Definition.—A chronic infective granulomatous disease, produced by a specific bacterium, and characterised by lesions of the skin, nerves, and viscera eventuating in local anæsthesia, ulceration, and a great variety of trophic lesions. After a long course it is almost invariably fatal.

History.—The many allusions in the oldest Chinese, Indian, Syrian, and Egyptian writings to a chronic, disfiguring, and fatal affection possessing well-marked and characteristic skin lesions, warrant us in concluding that the disease now known as leprosy was as common and familiar in the East in times of remotest antiquity as it is at the present day.

There is some evidence—necessarily of a negative character—that leprosy is of comparatively recent introduction into Europe. The earlier Greek and Latin writers do not mention the disease. Hippocrates, who, had he been practically acquainted with leprosy, would undoubtedly have described it accurately and fully, makes but brief allusion to the subject. Aristotle is the first of the Greek writers to give an unequivocal description. We may infer, therefore, that the introduction of leprosy into Greece probably took place between the time of Hippocrates and that of Aristotle—that is to say, between 400 B.C. and 345 B.C. Most likely it came from Egypt. In the time of Celsus—53 B.C. to A.D. 7—it was still a rare disease in Italy; but, during the earlier centuries

of our era it increased there, and, probably extending in the wake of the Roman conquests, it appears to have spread thence over the greater part, if not over the whole, of Europe. By the end of the seventh century it was well known in Spain, France, and Lombardy. There is a notice of its occurrence in Ireland in 432. As regards England, the first allusion to leprosy refers to about the year 950. The popular idea that it was brought to this country from the East by the returning Crusaders (*circa* 1098) is therefore incorrect; though, doubtless, the Crusaders, and the multiplicity of pilgrimages so much the fashion in the Middle Ages, and the destitution arising from the many wars of the period, had something to do with its rapid diffusion and great increase about this time.

So common was leprosy during the Middle Ages that the rulers and clergy of nearly all European States, becoming alarmed at its rapid extension and terrible ravages, took measures, by instituting leper asylums and enacting stringent laws for the segregation and isolation of lepers, to restrict the spread of what was speedily becoming almost a general calamity. These measures, based on what we now know to be a correct appreciation of the infectious nature of the disease, were ultimately crowned, in the case of most European countries, by almost complete success. Reaching its acme during the fourteenth century, leprosy then began gradually to decline, although as regards Great Britain it did not finally disappear as an indigenous disease until the end of last century. It died out first in England, later in Scotland—the last British leper dying in Shetland in 1798. In Italy, France, Spain, Germany, and Russia the repressive measures were almost equally successful, although in these countries, in Greece, and in the Greek islands leprosy of indigenous origin is still occasionally to be seen. The only country in Northern Europe in which at the present day it may be said to linger to any extent is Norway, where, in places, it is still by no

means uncommon (in 1890 there were 1,100 known lepers); but even here, under a system of segregation and comparative isolation—more humane perhaps in its application than that practised by our ancestors, although identical with it in principle—the disease is rapidly dying out.

Apart from Egypt, we know nothing of the early history of leprosy in Africa. We are equally ignorant as regards aboriginal America. The historians of the Spanish conquest do not allude to it as a native disease; we appear, therefore, to be justified from this circumstance in concluding that the introduction of leprosy into the New World was probably effected through the negroes in the days of the slave trade.

Rise of modern knowledge of leprosy.—The more important landmarks in our modern knowledge of leprosy are, first, the publication in 1848 of Danielssen and Boeck's *Traité de la Spedalskhed*, in which, for the first time, the clinical features of the disease were carefully and critically described; second, the descriptions of the macroscopic and microscopic lesions—the leproma, the nerve lesions, and the lepra cell—by Virchow, Vandyke Carter, and many others; and last, the discovery in 1874 by Armauer Hansen of the specific cause of leprosy—the bacillus lepræ—a discovery which brings this disease into line with tubercle, and which has given a much-needed precision to our ideas on the important subjects of heredity and contagion, and on other practical points bearing on the question of the leper as a source of public danger and on his treatment and management.

Geographical distribution.—Whatever may have been the case formerly, at the present day, with unimportant exceptions, leprosy is a disease more particularly of tropical and sub-tropical countries. So generally is it diffused in these that it would be more easy to specify the tropical countries in which leprosy has not, than to enumerate those in which it has, been ascertained to exist. Moreover, it is probable that in many of the countries not yet

positively known to harbour the disease it does really exist; for experience shows that the endemic area of leprosy enlarges as our knowledge of the natives of the uncivilised regions of the earth becomes more intimate. It may be safely concluded, therefore, that with the exception of a few insignificant islands, leprosy is an element, and often an important element, in the pathology of nearly all warm countries.

The only tropical country of any magnitude about which we have anything like accurate leprosy statistics is India; and even in this instance the figures, for many reasons—principally errors in diagnosis and concealment—are untrustworthy. According to the census of 1891, after making allowance for error, it is estimated that in British India there were 105,000 lepers in a population of 210,000,000—a ratio of about 5 in 10,000. Respecting China, of all countries probably the one in which there is the largest number of lepers, we have no figures to go by, but, judging from what is seen in the coast towns and treaty ports, the number of lepers there is even greater than in India. In Japan, in the Philippines, in Cochin China, in the Malay peninsula, in the islands of the Eastern Archipelago, and in several of the South Pacific islands, in Persia, Arabia, and Africa, the disease is common enough. The same may be said of the West Indies and of the tropical regions of America.

As regards more temperate countries, we know that there is a considerable number of lepers at the Cape, a few in Australia (principally Chinese but also a few Europeans), a few in San Francisco (Chinese). In Canada and in the United States there are also a few lepers of European blood, but their number is quite insignificant. In New Zealand, where leprosy was at one time common among the Maoris, it has died out. There are a good many lepers in Iceland. It is also reported as existing among the aborigines of the Aleutian peninsula and Kamschkatka. In Great Britain and

other European countries, particularly in the capital cities, lepers are not infrequently exhibited at medical societies, but, with rare exceptions, these cases are not of indigenous origin, most of them having contracted the disease abroad

Though thus extensively diffused, leprosy is by no means equally prevalent throughout the wide area indicated. Thus in China it is comparatively rare in the northern provinces, excessively common in the southern. In India a similar caprice of distribution is noted; in Burdwan, for example, the proportion of lepers in 10,000 of the population is as high as 19·5, whereas in several other districts it is as low as 1·5, or even lower. This caprice of distribution does not seem to depend on climate, geological formation, or suchlike physical conditions, leprosy is found in mountainous districts, on the plains, on the coast, in the interior, in all varieties of climate, and on all kinds of geological strata. Social conditions, it would seem, have most to do in determining distribution; its endemic prevalence appearing to be bound up in some way with uncleanly habits, squalor, dirt, and poverty —not, be it noted, directly caused by these things, but associated with them.

Recent introduction. An interesting and, from the ætiological standpoint, an important circumstance about the geographical distribution of leprosy is its appearance in recent times and rapid spread in certain islands whose inhabitants, there is good reason to believe, had previously been exempt. This modern introduction of leprosy into virgin soil, so to speak, has taken place in two islands at least the Sandwich Islands and New Caledonia.

Sandwich Islands.—In the case of the Sandwich Islands leprosy was noted among the aborigines for the first time in 1859. After the most painstaking investigation Dr. Hildebrand failed to trace it farther back than 1848. Soon after its presence was recognised the disease spread so rapidly that by the year 1865 there were 230 known lepers in a population

of 67,000. By 1891 the native population, from various causes, had diminished to 44,232; of these 1,500 were lepers—about 1 in 30.

New Caledonia. In New Caledonia (Grall, *Arch. de Méd. Navale*, Oct., Nov., Dec., 1894) leprosy was unknown until 1865. It is supposed to have been introduced about that time by a Chinese; the man was well known. Its rapid diffusion throughout the island can be, and has been, traced step by step. In 1888 the lepers numbered 4,000.

Isles of Pines. Similarly, in the Isles of Pines it was introduced in 1878, and has since spread. In the Loyalty Islands the first case was seen in 1882; in the island of Mare alone in 1888 there were 70 lepers.

Symptoms.—Although, as will afterwards be explained, the bacillus lepræ is the cause of all leprosy, the clinical manifestations of its presence are far from being identical in every case; indeed, they are almost as varied as are those of syphilis or of tubercle. Our early conceptions of the disease, derived for the most part from the Bible or poetical literature, in which the leper is symbolical of all that is loathsome and hopeless, are apt to mislead. As a matter of fact, in its earlier stages leprosy is far from being always, or even generally, a striking disease. Often for years the only visible evidence of its existence may be two or three small blotches, or perhaps one or two patches of pale or pigmented skin about trunk or limbs—very likely concealed by the clothes and perhaps disregarded by the patient himself—whose true significance and nature can be appreciated only by the expert. It is generally not until the later stages that we see the disfiguring and extensive lesions on which the popular conception is founded. As a rule, leprosy is a disease of very slow development. Sometimes, it is true, it is suddenly and frankly declared from the outset, and progresses rapidly; but, in the vast majority of cases, the early lesions are trifling and are apt to be misinterpreted and overlooked, and years elapse before serious

mutilation or deformity is produced. The student must bear this important practical fact in mind in the study and diagnosis of all equivocal skin lesions in persons residing in, or coming from, the endemic haunts of leprosy.

To facilitate description, it seems advisable to divide the evolution of leprosy into stages, premising, however, that the division proposed is in great measure an artificial one. What are here designated stages are not, all of them, in nature and in every instance, abruptly separated or even present; for the most part they merge imperceptibly into each other and, in not a few instances, some of them cannot be recognised.

1. The primary infection.
2. The period of incubation.
3. The prodromata.
4. The primary exanthem or macular stage.
5. The period of specific deposit.
6. The sequelæ — ulceration, paresis, trophic lesions.
7. Terminations.

1. *The primary infection.*—Seeing that leprosy is caused by a specific germ, there must have been a time in the history of every leper when the infecting germ entered the body. In the case of many specific diseases, such as syphilis, the site of the primary infection is indicated by a well-marked local lesion and the time of infection can usually be ascertained. So far as present knowledge goes, this much cannot be affirmed of leprosy; in this disease we know of nothing that indicates either the seat or, with rare exceptions, the time of primary infection. In this respect leprosy resembles tuberculosis. We are equally ignorant as to the condition of the infecting germ, whether it enters the organ or organs through which it gains access as spore or as bacillus; and, also, as to the medium in or by which it is conveyed. We cannot say whether it enters in food, in water, in air;

whether it passes in through the unbroken epithelium, or whether it is inoculated on some accidental breach of surface, or, perhaps, introduced by some insect bite.

But though we are in absolute ignorance as to the process of infection, we may be quite sure that in leprosy there is an act of infection, and that the infective material comes from another leper. Leprosy has never been shown to arise *de novo*. There are many facts and arguments to support this statement; their discussion is deferred until the important practical subjects of heredity, contagion, and the hygienic questions connected therewith come to be considered.

2. *The period of incubation.*—This is generally, possibly always, long, and has to be reckoned usually in years—two or three at least. There are cases on record in which the period of incubation must have been longer even than this. Danielssen mentions one in which the period was ten years. Leloir describes another in which fourteen years or more, and Höegh one in which twenty-seven years, elapsed between the time at which infection was presumed to have occurred and the first manifestations of the disease. On the other hand, cases are on record in which the incubation period was set down at three months or even at a few weeks.

3. *Prodromata.* — Fever of greater or less intensity, and occurring more or less frequently is, almost invariably, a feature of the prodromal stage of leprosy. Febrile attacks may recur off and on during one or two years. It is well to bear in mind that in tropical countries such attacks are apt to be looked on as malarial. Another very common prodromal feature is an unaccountable feeling of weakness, accompanied usually by a sensation of heaviness and a tendency, it may be irresistible, to fall asleep at unusual times. Dyspeptic troubles, associated with diarrhœa in some cases, with constipation in others, and usually attributed to "liver," are also common. Epistaxis and dryness of the nostrils,

corresponding to the epistaxis in the prodromal stage of typhoid, tuberculosis, and such as is sometimes met with in early syphilis, are noted by Leloir. This epistaxis must not be looked upon as resulting from actual leprous rhinitis, which is a feature of a later stage of the disease. Headache; vertigo, perversions of sensation such as localised pruritus, hyperæsthesia, "pins and needles," neuralgic pains—intermittent for the most part, and perhaps very severe and especially common in the limbs and face; general aching, rheumatic-like pains in loins, back, and elsewhere; all or any of these for months before may herald the explosion of leprosy. They point to a direct and early implication of the nervous system by the lepra bacillus, or to a toxin poisoning by its products.

Another curious feature in early leprosy, also noted by Leloir, is the liability in many instances to excessive sweating, which comes on without apparent, or on very slight, provocation. I had once under observation an Englishman who subsequently developed leprosy, in whom this prodromal symptom was particularly pronounced, so pronounced that he had remarked it himself. This gentleman for many years kept a diary in which, among other things, he recorded very carefully matters relating to his health; so that it was easy to trace from this diary the gradual evolution of his leprosy. The first unequivocal manifestation of the disease, an extensive erythematous patch on the ulnar side of the left arm and hand, which afterwards became anæsthetic, and two or three pigmented spots on the cheek, back, and leg, was noted on March 3rd, 1894. Five years before this there is an entry in his diary, under date June 4th, 1889, of the first of a long series of severe headaches, transient febrile attacks, and progressive deterioration of health and vigour. Under date of June 9th, 1892, is the first mention of the profuse perspiration which, occurring without obvious cause, continued to be a prominent feature until several months after the appearance of the skin lesions

referred to. In the diary such entries as the following frequently occur: "Nov. 20th, 1892. —Feel poorly and sweating inordinately; wondering what is coming over me. I am very ill." "Dec. 5th to 19th, 1892. Ill in bed. I had furious sweats during this time, and had dreadful pains in the back, lower part." And again, "Dec. 21st, 22nd. Feeling very ill; awful sweats; weak; done up." As pointed out by Leloir, this hyperidrosis may be general or it may be confined to particular parts, generally the trunk, the limbs being unaffected or even being the subject of anidrosis. A still more limited anidrosis is sometimes noted; it usually happens that these non-sweating spots become anæsthetic at a later period of the disease.

It is well to bear in mind that, just as in syphilis, in a very small proportion of cases of leprosy there is a complete absence of constitutional symptoms prior to the appearance of the specific skin eruption. Such cases do occur, although they are distinctly rare.

4. *The primary exanthem.*—After a longer or shorter period of indifferent health, and being sometimes preluded by an outburst more severe than usual of fever and other prodromic phenomena, an eruption appears on the skin. The occurrence of this generally coincides with, or is soon followed by, an improvement in the general health.

Although strictly macular, this eruption the primary exanthem of leprosy varies in different cases both as to the size of the spots, their number, duration, and other characteristics. They may be no larger than a millet seed, or they may occupy surfaces many inches in diameter, they may be numerous, or there may be only two or three. The earlier spots are usually purely erythematous, disappearing on pressure, and being darkest in the centre and shading off towards the periphery. But in some cases they may be pigmented from the outset; or they may be mere vitiliginous patches; or all three forms of macula may concur in the same individual—erythematous,

pigmented, and vitiliginous. In not a few lepers what in the first instance was an erythematous patch may in time become pigmented, or it may become pale; in the latter case the loss of pigment is usually associated with a certain degree of atrophy of the cutis. Or it may be that the centre of an erythematous patch clears up, the periphery of the patch remaining red and perhaps becoming pigmented; so that the affected spot comes to present the appearance of a red or dark ring, or portion of a ring, enclosing a patch of pale, usually anæsthetic skin. In certain instances the eruption of the various forms of maculæ may be preceded by local paræsthesiæ, such as a sense of burning, tingling, pricking, and so forth.

At first the maculæ may be evanescent and may fade wholly or in part in the course of a few days, weeks, or months; but as the disease progresses, and fresh spots appear, they tend to greater permanency, to be more liable to pigmentation, and are partially or wholly anæsthetic from the outset, or subsequently become so.

A striking feature in this and in all leprous eruptions is the loss of the hair in the affected areas. Another striking circumstance in this connection is the fact that the most hairy part of the body, the scalp, is never affected either with leprous eruptions or with what could be considered leprous alopecia. As the face, particularly the superciliary region, is prone to all forms of leprous eruption, falling of the eyebrows is a very usual, very early, and very characteristic phenomenon. The beard, too, is apt to be patchy, particularly in nodular leprosy. In many instances, before they drop out, the individual hairs become white, or downy, or splintered, or monillated.

The most frequent seats of the primary macular eruption are the face, especially the superciliary region, the nose, cheeks, and ears; the extensor surfaces of the limbs; the backs of the hands; the back, buttocks, abdomen, and chest. The palms of the hands and the soles of the feet are rarely if ever

attacked; the scalp never. At this stage of the disease the mucous membranes are very rarely affected.

In the distribution of the maculæ a rough symmetry may or may not be discernible.

3. *The period of specific deposit.*—During the stage just described, if there be any thickening of the skin or other evidence of new growth, it is barely perceptible to sight and but slightly to touch. Sooner or later, however, another stage is entered on, a stage characterised by the deposit or, rather, growth of a tissue possessing well-marked specific characters. This deposit occurs either in the skin, or in the continuity of the peripheral nerve trunks, or in both. If in the first situation, nodular or, as it is sometimes called, tuberculous leprosy is the result: if in the second, we have nerve or anæsthetic leprosy; if in both of these situations, then what is known as "mixed leprosy" is produced. These three forms of the completely developed disease, though having much in common, are, as a rule, clinically fairly distinguishable. It is customary, therefore, to describe them separately.

NODULAR LEPROSY.

This form of leprosy often appears without a preliminary well-marked macular stage, being ushered in, after a longer or shorter prodromic stage, by a smart attack of fever and the rapid development on the face or elsewhere of the specific lesion. In other instances a well-defined but, in comparison with nerve leprosy, short macular stage precedes the appearance of the characteristic lepromata (Fig 30).

The essential element in nodular leprosy is the leproma. The dimensions, the combinations, the situations, the growth, and the decay of this give rise to the more manifest symptoms of the earlier stages, at all events, of the disease. The leproma, which will be more fully described in the section on the pathological anatomy of leprosy, is formed by infiltration of the deeper layers of the derma with what

Fig. 80. Nodular Leprosy (*Lebour*).

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The essential element in nodular leprosy is the leproma. The dimensions, the combinations, the situations, the growth, and the decay of this give rise to the more manifest symptoms of the earlier stages, at all events, of the disease. The leproma, which will be more fully described in the section on the pathological anatomy of leprosy, is formed by infiltration of the deeper layers of the derma with what

Fig. 80. Nodular Leprosy (*Lefour*).

at first is a small-celled, somewhat dense neoplasm. As this slowly or more rapidly increases it forms a prominent, rounded boss or protuberance covered with unbroken epidermis. In size it ranges from the dimensions of a split pea, or of a bean, to a great plaque many inches across. In colour it is different according to its age and condition, and according to the natural hue of the skin of the leper; it varies from red to dirty pink in the earlier and congestive active stage, to dark brown or dirty yellow in the later stages. It is generally, though not always, especially at first, anæsthetic to some degree, if not absolutely so; it is devoid of hair, usually somewhat greasy-looking and, perhaps, stippled with gaping follicles. Though not so hard as keloid growth, it is fairly firm to the touch, and, unless very extensive, can be readily raised up and freely moved over subjacent structures. Isolated lepromata are usually round or oval; when contiguous they may coalesce, forming patches of irregular outline.

When many lepromata run together, or are closely set, the growth causes the natural folds of the skin to be exaggerated; and thus great disfigurement, especially of the face, may ensue. Thus the skin of the forehead and eyebrows—an early and favourite site of leprous infiltration—is thrown into massive folds and overhangs the eyes; the fleshy parts of the nose broaden out; the cheeks become massive; the lips are thickened and protrude; the chin is swollen and heavy; the external ears are thick and pendulous; and the bloated, dusky, wrinkled, greasy, passive countenance acquires the repulsive appearance very appropriately designated "leontiasis."

Nodules may appear in greater or less profusion on the limbs and body; favourite sites being the backs of the hands, the external surfaces of the arms, wrists, thighs, and the groins. On the trunk they may occupy very large areas, forming extensive plaques. As a rule, in the latter situation they are not so prominent as on the face and arms. The same remark

applies to the legs, where the infiltration is usually dusky, diffuse, ill-defined, and prone to ulcerate.

From time to time, and at longer or shorter intervals, fresh tubercles appear, their formation generally concurring with an outburst of leprous fever. Occasionally, and this is very often observed during an intercurrent attack of some acute disease —such as an exanthematous fever, or erysipelas, or even of some exhausting disease like phthisis—all or a proportion of the nodules are temporarily absorbed, leaving only slight traces behind. But the normal and usual fate of the nodule is either first to soften in the centre and then to be absorbed, leaving a smooth circular patch of scar tissue; or, after softening, to ulcerate and discharge a sticky, yellowish pus. This discharge tends to dry up into crusts, ulceration proceeding underneath. Finally the ulcer may heal, leaving an irregular, depressed scar.

When the mucous membrane of the nose is affected, as it usually is in time, the cartilage of the septum breaks down, the tip of the organ becoming depressed, and a stinking discharge escapes from the nostrils. In such circumstances breathing is very much interfered with, more especially if, at the same time, leprous deposit occurs or ulcerates in or about the glottis, the epiglottis, pharynx, tongue, or mouth generally. The senses of smell and taste are then lost for ever.

The eyes, also, are sooner or later attacked, lepromatous growth spreading from the conjunctiva on to the cornea or into the anterior chamber, or originating in the iris or ciliary body. Ultimately this organ also is destroyed, and with it the sense of sight.

Thus, in time, with the exception of that of hearing, one sense after another disappears. Ulcers form everywhere from the breaking-down of the nodules or from injuries to the insensitive skin. The cervical and inguinal glands, owing to leprous infiltration, swell and perhaps suppurate and become fistulous; the abdomen enlarges from leprous, perhaps combined with amyloid, infiltration of the liver, and there

may be diarrhœa from amyloid disease of the intestine. In addition to these troubles, if the patient live, the nerve trunks are attacked, and then the neuralgic, paretic, and trophic lesions of nerve leprosy are superadded. The fingers and toes ulcerate and drop off, or they become distorted and atrophied; or the phalanges are absorbed, the hands and feet becoming reduced to useless stumps. A peculiar goat-like smell is emitted by the ulcerating, decaying body. Altogether, the blind, lame, unhappy wretch still retaining his intellect but devoid of every sense except that of hearing, breathing with difficulty through a stenosed larynx, and racked by neuralgic pains and irregular outbursts of fever—comes to present, before the inevitable death from exhaustion occurs, a sadder, more loathsome, and more repulsive picture than imagination could conceive. Fortunately, in a large proportion of cases, the leper is mercifully carried off by phthisis, pneumonia, or some intercurrent affection at an earlier period, and before his disease could be said to have run its full course.

NERVE LEPROSY.

Just as in nodular leprosy, in nerve leprosy the prodromic and macular stages may be severe, or slight, or altogether absent. Usually, however, in nerve leprosy, much more frequently than in nodular leprosy, the ulterior and more distinctive lesions are preluded by a long and well-marked macular stage, during which large areas of skin are occupied by erythematous (Fig. 31), by pigmented, or by vitiliginous patches. The ringed form of eruption is a very usual one; a red, congested, slightly elevated and, perhaps, hyperæsthetic border enclosing a larger or smaller area of pale, anæsthetic, non-sweating integument the whole resembling somewhat one of those extensive body ringworms so common in natives of hot, damp climates, for which these rings are sometimes mistaken. Such eruptions may come and

Fig. 31.—Nerve Leprosy (*Leoir*).

go, or they may be permanent, or they may spread and multiply during many years before the more distinctive and graver signs of nerve leprosy are evolved.

A frequent and very distinctive symptom of this type of the disease, occurring often about this time, is the sudden appearance of bullæ (*pemphigus leprosus*) —one or more or a series of them—on the hands, feet, knees, backs of thighs, or elsewhere. These bullæ vary in size from a pea to an egg. After a few days they rupture, exposing a reddish surface which presently crusts over, exfoliates, and finally turns into a pale, perhaps anæsthetic, spot with a sharply defined, pigmented border. More rarely the site of the bulla ulcerates. Should similar bullæ be formed in the neighbourhood of the first, the resulting ulcerations may unite into an extensive, probably superficial, serpiginous-looking sore.

A time comes when evidence of profound implication of the nervous system, in the shape of severe neuralgic pains, formication, hyperæsthesia, or anæsthesia, becomes more accentuated. The lymphatic glands enlarge, and there is often considerable fever and general distress. Hitherto, the most prominent symptoms have been the skin lesions. These may remain or even increase; on the other hand, they may in part or entirely disappear. But whether the skin lesions increase or retrograde, evidences of profound implication of the peripheral nervous system now distinctly show themselves; the neuralgic pains still further increase, and hyperæsthesia, anæsthesia, and various paræsthesiæ, along with trophic changes in skin, muscle, and bone, the results of nerve destruction, become the dominating elements in the case.

If at this stage the ulnar nerve where it passes round the internal condyle of the humerus be examined, generally it will be found to be the seat of a fusiform swelling perhaps as thick as the little finger. Other nerves, such as the anterior tibial, the peroneal, more

rarely the median, radial, brachial, and cervical nerves, especially where they pass over a bone and lie close under the skin, can be felt to be similarly swollen. Occasionally even the smaller nerves, where superficial, can also be detected hard and cord-like. At first these thickened nerves are tender on pressure, and the parts they supply may be the seats of hyperæsthesia and acute neuralgia. By degrees, however, the great thickening of the nerve trunks decreases somewhat, the hyperæsthesia and neuralgia subside, and anæsthesia and muscular atrophy and other trophic changes, with paresis, take their place. For a time the condition may fluctuate; the neuritis apparently may come and go with corresponding changes in the condition of the area subserved by the affected nerves. Sooner or later, however, fibrotic changes ensue in the neural leprous deposits, the nerve tubules ultimately atrophying and disappearing. The nerve tissue is now irreparably damaged, and trophic changes steadily advance. In other instances, anæsthesia comes on without neuralgic pains, without hyperæsthesia, without constitutional symptoms, without discoloration of the skin, the patient discovering its existence by accident.

In nerve leprosy, the anæsthesia begins most commonly in the feet, the thighs, hands, arms, forearms, and face. Later, and more rarely, it affects the trunk. The anæsthesia, though associated with well-marked lesions of the larger nerves, does not always, or even as a rule, coincide accurately with the anatomical distribution of their terminals; a circumstance which tends to show that the anæsthesia is not always and simply the result of lesion of nerve trunks, but that it may be the effect of the destruction by the bacillus of the nerve terminals themselves; a suggestion which is strengthened by Gerlach's discovery that in anæsthetic leprosy the bacilli appear first in the skin around the nerve terminals, and only subsequently extend upwards to the nerve trunks. Another, and sometimes a

very striking, fact in nerve leprosy is the symmetry observed in the distribution of some of the anæsthetic areas. This symmetry is by no means invariable; in not a few cases, however, it is very perfect and remarkable.

At the outset the anæsthesia in the affected patches may not be absolute; it may also come and go, and it may be very superficial, deep pressure being for a long time appreciable. But when the anæsthesia becomes, as it were, settled in a part, it seems gradually to extend deeper into the tissues; so that after a time it is absolute, and the parts may be pinched, incised, and even seared with fire, and the leper be absolutely unconscious of pain or even of being touched.

Step by step with the progress of the anæsthesia, atrophy of the subjacent muscles supplied by the thickened nerves proceeds. Along with the atrophy there is a corresponding distortion and a corresponding loss of power. There is no ataxia or inco-ordination of movement; simply feebleness. Thus the forearm wastes, the grasp is weakened, the thenar and hypothenar eminences, and the interossei melt away, and the *main en griffe* or some such deformity is gradually produced (Fig. 32). Similar changes occur in the legs and feet, so that the power of walking is much impaired. The muscles of the thighs and upper arms, the pectorals, and the muscles of the face follow suit, very much as in progressive muscular atrophy, only in the latter there is no superjacent anæsthesia.

In the affected nerve areas all the muscles are not simultaneously or equally attacked, so that, especially in the face, curious distortions may ensue. These facial atrophies, whether symmetrical or one-sided, in time produce a facies as characteristic of nerve leprosy as leontiasis is of nodular leprosy. From muscular atrophy the eyes after a time can no longer be closed; the upper lid droops, the lower lid becomes everted, and the eye itself may become fixed. At first, owing

Fig. 32.—Nerve Leprosy : Main en griffe (*Leloir*).

to exposure of the organ, there is lachrymation, but by-and-by the secretion of tears dries up, the congested conjunctiva becomes cornified, the cornea ulcerates or turns leucomatous, and in the end sight is entirely lost. Ulceration often occurs in the mucous membrane of the nose, the septum being destroyed as in the nodular form; the tip of the nose may then be lost or it falls down. The lips, too, may become paralysed, interfering with articulation and permitting the saliva to dribble from the mouth in a constant stream. Changes occur, too, in the mucous membrane of the mouth; the gums may retract, exposing the maxillary bone, the teeth ultimately dropping out. Anæsthesia of the tongue and buccal mucous membrane, and implication of the muscles of mastication may render eating and articulation very difficult.

In time the skin of anæsthetic patches on the limbs tends to atrophy; it loses its glands and hairs, and, in the end, may become so thinned and tense that it may actually burst into long cracks. The nails are not generally shed, but they become rough or thinned or atrophied into minute, hook-like appendages.

Ulcers form over exposed parts of the hands and feet. They may penetrate and disorganise the joints, and thus often cause fingers and toes to drop off, one after another. Or, perhaps, an abscess forms around a phalanx, destroys the periosteum, and ultimately leads to loss of the bone. Or a sort of dry gangrene may amputate finger or toe. Or there may be a curious interstitial absorption of one or more phalanges, the shaft of the phalanx wasting more rapidly than the articulating surfaces. In any of these ways the fingers and toes are distorted or destroyed. It is no unusual thing to see on a leper's hand a finger in which one or more of the phalanges have been thus got rid of without destruction of the fleshy part, or with only a general shrinking of this. Thus it comes about that a distorted, talon-like nail may crown a finger which is a mere stump; or, the finger

having been entirely absorbed, the nail springs, as it were directly, from the knuckle.

Perforating ulcer of the sole of the foot, as might be expected, usually under the ball of the great toe or the heel, is a very common lesion in nerve leprosy.

On the whole, the advance of this form of leprosy is much slower than that of the nodular variety. The average duration of the latter is from eight to nine years, of nerve leprosy about eighteen years. Often such lepers live much longer—twenty, thirty, or even forty years. As can readily be understood, the end of these cases is quite as sad and repulsive as it is in nodular leprosy. Death seldom results directly from the disease itself; diarrhœa, chronic nephritis, phthisis, pneumonia, or bronchitis being, one or other of them, usually the immediate cause of death.

MIXED LEPROSY.

As already explained, in most cases of nodular leprosy, trophic changes from implication of nerve trunks ultimately supervene. Similarly, though not so frequently, nodular infiltration of the skin may appear in the course of what originally seemed to be a case of pure nerve leprosy. In yet other cases nodular and nerve lesions concur from the outset of the disease. In one or other of these ways what is known as mixed leprosy is produced. The lesions are in no way different from those already mentioned, and therefore this form of the disease does not call for more detailed description.

Pathological anatomy. — *Bacillus leprœ.* — The lesions of leprosy are the result, direct or indirect, of the proliferation of the bacillus lepræ in the tissues. This parasite (Fig. 33) in size, shape, and staining reactions closely resembles the bacillus of tubercle. In length it is from half to two-thirds, and in breadth about one-sixteenth the diameter of a blood-corpuscle. The ends of the rod—which is always straight—are in many specimens somewhat

attenuated; and in many instances — presumably in old bacilli — a moniliform arrangement of the protoplasm, as if from spore formation or, according to Hansen, from disintegration, can be detected. By some authorities it is said to possess a gelatinous capsule. From bacillus tuberculosis it may be distinguished by the somewhat greater difficulty with which the stained specimen is decolourised by acids; by the impossibility hitherto experienced of growing

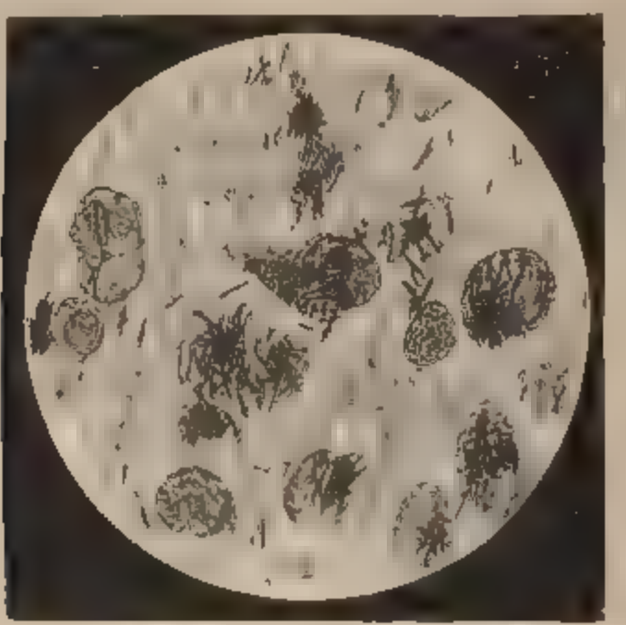

Fig. 93. Bacillus lepræ. × 1000 (*Murrison Hitchie*).

it on the usual, or on any culture media, and of inoculating it in man and the lower animals, by its tendency to occur in dense clusters; and by its very generally being found inside cells or, according to Unna, in zooglœa masses in the lymphatic spaces.

Specimens of the bacillus can be procured readily by excising a portion of a leproma—a proceeding, in consequence of the absence of sensation in most tubercles, not usually much objected to by lepers; or they may be obtained by including a succulent leproma in a pile clamp, slowly screwing up the jaws of the instrument so as to drive out the blood,

pricking the now pallid leproma, and then collecting on a cover-glass the droplet of "leper juice" which exudes from the puncture. The juice may be spread out on the cover-glass, fixed, stained, and decolourised as for the demonstration of tubercle bacilli, or it may be examined fresh.

If examined fresh, or if a morsel of leproma be teased up in water, the bacilli may be seen both inside and outside the cells and in active motion. Whether this motion is simply molecular, or whether it is vital, it is hard to say; probably the former, for, whilst osmic acid does not stop it, it is immediately arrested by the addition of viscid fluids, such as glycerine or albumin water.

The bacillus is found in all primary leprous deposits; in the skin leproma—where it occurs in prodigious numbers; in the meagre infiltration of the macular eruptions where it is much more sparsely distributed; in the early stage of leprous neuritis—where, also, it is present only in small numbers; in the specific lesions of the liver, spleen, testes, and lymphatic glands. In the blood-vessels it has been found in the endothelium and, occasionally, free in the blood or enclosed in leucocytes. It is abundant in the purulent discharges from ulcerating lepromata or other forms of primary leprous infiltration. It has very rarely been found in the spinal cord or in the lungs. It is doubtful if it occurs in the brain, the intestinal tract, or in the kidneys, although the latter are prone to inflammation in leprosy. It is not found in muscle, in bone, or in cartilage; and it is not necessarily present in the secondary trophic lesions of nerve leprosy, or in secondary inflammatory effusions.

The leproma. The young leproma presents a smooth, white, glistening section. When the leproma is older the cut surface has a brown tint, and the morbid tissue may become, from fibrotic changes, harder, or, from degeneration, softer. The specific lesion of leprosy differs from that of tubercle, inasmuch as it is well supplied with blood vessels, contains no giant cells

(Hansen), and never undergoes caseation. If hardened, cut, stained, decolourised, and examined under the microscope, the leproma is found to consist principally of small round cells about the size of a leucocyte, epithelioid cells, and fusiform cells the two latter in increasing numbers with the age of the leproma. It can be seen that these cells have infiltrated and partially dissociated all but the most superficial layer of the derma. It may be further observed that the cells are arranged for the most part in groups, generally around and near blood-vessels; and that a very large proportion of them contain bacilli, some cells having only a few, whilst others are literally crammed with the parasites. Isolated bacilli are also found scattered through the preparation, apparently free in the lymph spaces. The bacilli are never seen inside the nuclei of the implicated cells.

In addition to the bacilli bearing cells, and increasing in number with the age of the lesion, a number of brown granular bodies, larger and smaller, which have been named "globi," are to be found. These Hansen holds to be cells in which the bacilli have perished and become granular. It is to them that the brown colour of old lepromata is due.

There has been considerable discussion as to the exact position of the bacilli as regards the lepra cells —whether they lie inside the cells or whether they are free. On the one hand, Unna holds that they lie free in the lymph spaces, and that they are never in the cells, the appearance of cell inclusion being produced by the zoogloea arrangement so common with bacteria. On the other hand, Leloir maintains that some of the bacilli are free, whilst others are inside the cells. A third set of observers, following Hansen, hold that the bacilli are almost invariably included within cells the nuclei of which can readily be demonstrated surrounded by the parasites.

Other lesions. The histology of the infiltrated macula is practically the same as that of the leproma, the number of bacilli, lepra cells, and globi being

proportionately fewer. In old maculæ, as in very old lepromata, the bacilli may be hard to find or entirely absent. In the anæsthetic maculæ the terminal nerve fibres are degenerated.

As the fusiform thickening of the larger nerve trunks in nerve leprosy is a secondary inflammation, bacilli may not always be found in it, although at the very commencement of the nerve disease bacilli, both in cells and, according to Leloir, free between the nerve tubules, are present and may even lie in the nerve tubules themselves. In time the affected nerves become mere fibrous cords destitute of nerve tubules.

The anatomy and histology of the various trophic lesions are such as are found in other examples of destructive neuritis, and are in no way peculiar to leprosy; they do not, therefore, call for description here.

In nodular leprosy the liver and spleen are the subjects, in many instances, of a peculiar infiltration which, in well-marked examples, may be visible to the naked eye. Fine yellowish-white dots and streaks are seen to occur in the acini of the former. These dots and streaks consist of new growth in which bacilli abound; according to Leloir, the parasites are never found in the hepatic cells themselves.

In all cases of nodular leprosy the testes atrophy and undergo fibrotic changes, bacilli and globi being found both in and around the tubules, free and in cells.

In all forms of leprosy the lymphatic glands appertaining to parts in which leprous deposit is present are characteristically affected. They are swollen and hard, and on section the gland tissue is seen to have a yellowish tinge from an infiltration which contains numerous bacilli and globi.

Albuminoid disease of the alimentary canal, liver, and spleen, and nephritis occur in a large proportion of the cases of nodular leprosy.

Diagnosis.—The touchstone in all doubtful cases is the presence or absence of anæsthesia in some skin

lesion or in some skin area. Anæsthesia is rarely absent in leprosy; generally, in the implicated spots, it is complete, or nearly so. It should be particularly sought for towards the centre of maculæ, in the pale patches left after the fading of former maculæ, in the hands and feet, and in nodules of some standing. In no other skin disease is definite anæsthesia a symptom. Vitiligo, or leucoderma—sometimes called white leprosy, and by the vulgar very generally regarded as true leprosy—bears a certain resemblance to the pale post-macular patches referred to; not to mention other features, the absence of anæsthesia in leucoderma at once settles diagnosis.

Further assistance may sometimes be got in doubtful cases from the fact that leprous spots rarely perspire. A hypodermic injection of pilocarpine is of use in bringing out this point.

The sensory and trophic lesions of syringo-myelia might be mistaken for nerve leprosy; but the general history of the case, the history or presence of macular eruption, of thickened nerve trunks, and of enlarged lymphatic glands in leprosy, and their absence in syringo-myelia, are mostly sufficient to establish a diagnosis.

It is hardly necessary to point out the diagnostic marks of leprosy as against syphilis, erythema multiforme, erythema nodosum, lupus vulgaris, lupus erythematosus, psoriasis, eczema, lichen planus, keloid, body-ringworm, erythrasma, pityriasis versicolor, elephantiasis Arabum, etc. Mistakes can scarcely be made unless from carelessness, or by some one completely ignorant of the nature, history, and symptoms of these diseases.

In approaching the diagnosis of skin eruptions, localised pareses, muscular atrophies, and anæsthesia in patients living in, or coming from, a country in which leprosy is endemic, the possibility of their being attributable to this disease must be borne in mind. If doubt exist, and it be found feasible, search should be made in eruptions or in thickened nerves

for the bacillus. If this is found the diagnosis of leprosy is infallibly established.

Prognosis.—Complete recovery is an event so rare in leprosy that, though it may be hoped for, it must not be expected. Recovery from the actual disease itself—that is, in the sense that fresh leprous infiltration may cease to occur, and old infiltration may be absorbed, and that the bacilli may die out—is perhaps the rule in nerve leprosy; but the effects of the leprous process are permanent, the trophic lesions resulting from nerve destruction being irremediable. Such cases may live, however, for many years—thirty or forty—and die of some other disease; at best, they are but mutilated specimens of humanity.

Nodular leprosy is usually a much more acute disease than nerve leprosy, sapping the strength and general health much more effectually and quickly. It rarely runs its full course, death being brought about by some intercurrent disease, such as, and especially, phthisis, nephritis, albuminoid degeneration of the alimentary tract, dysentery, stenosis of the larynx, and pneumonia. It may prove fatal as a sort of galloping leprosy within a year even of its first declaring itself.

Ætiology. *Age.*—It is open to question if leprosy has ever been seen in the fœtus. It has once or twice been reported in the newly-born. Cases are also on record of its occurrence as early as the first and second years of life; such, however, are quite exceptional. Leprosy is extremely rare before the fifth or sixth year. In the great majority of instances the disease begins between the tenth and thirtieth years. It rarely commences after forty, although it has been known to begin up to, and even after, seventy.

Sex, occupation; social and hygienic conditions. Sex, apart from the associated social conditions as affording opportunity for contagion, seems to have little bearing on the liability to leprosy. The same may be said of occupation, and social and hygienic

conditions in general. Very probably bad food and bad hygienic circumstances have in this, as in most germ diseases, a predisposing influence; but they certainly cannot create a lepra bacillus and leprosy any more than they can create an acarus scabiei and itch. This is abundantly demonstrated by the absence of leprosy at an earlier period in countries in which, without alteration in the food or other hygienic conditions, the susceptibility of the natives to the disease was subsequently proved by its rapid spread on being introduced from without, *e.g.* the Sandwich Islands and New Caledonia: and, also, by the disappearance of the disease, in other instances, under the influence of the segregation and isolation of lepers, without any concurrent material alteration in food or other circumstances, *e.g.* Scotland and Ireland and many other European countries.

Climate.—Climate can in no way be considered a cause of leprosy, for leprosy exists in all climates and in all latitudes. But it does seem to have some influence in determining, to a certain extent, the type the disease assumes. It would appear that the nodular form is more common in cold, damp climates, the nerve form in warm or dry climates.

The lepra bacillus.—Hansen remarks, "There is hardly anything on earth, or between it and heaven, which has not been regarded as the cause of leprosy." However true this remark may be as regards times prior to Hansen's discovery, we are now practically certain that the lepra bacillus is the cause of leprosy. The only gap in the evidence, otherwise conclusive, lies in our present inability to cultivate the bacillus, or to convey it by inoculation or otherwise to the lower animals, or, perhaps, to man himself.

Many attempts have been made to communicate leprosy to man by inoculation, but hitherto, with one questionable exception, all have failed. A Sandwich Islander, apparently at the time free from leprosy, was inoculated from a lepra tubercle. Within a month he had symptoms of leprous neuritis; two

years later he was a confirmed leper; and in six years from the date of the inoculation he died of leprosy. Unfortunately the subject of the experiment was a native of a country in which leprosy was extensively endemic; and besides, he had lived among lepers, in fact, members of his family were lepers. However possible it may be that the bacillus in this instance had been communicated by the inoculation, the circumstances in which the experiment was made, and the unusual shortness of the incubation period, are against its being regarded as conclusive evidence of the inoculability of the disease.

To bridge over temporarily this important gap in the evidence, we have to fall back on the close analogy that exists between the lepra bacillus and the bacillus tuberculosis, the leproma and the tubercle, leprosy and tuberculosis. In consideration of this and other circumstances, it is generally conceded nowadays that the bacillus lepræ is the true cause of leprosy, just as bacillus tuberculosis is the cause of tubercle. Authorities differ, however, as to the way in which the bacillus is acquired.

How acquired.—It is aburd to suppose that an organism of any sort, no matter how humble in the scale of life, can originate *de novo;* such an hypothesis may be at once dismissed. Disregarding this we have to consider two principal views entertained as to the way in which the bacillus is acquired—heredity and contagion.

Heredity.—From the fact that it tends to run in families and that it assumes the appearance of atavism in certain instances, leprosy, until the bacillus lepræ was discovered, was almost universally—as it still is by some—believed to be a hereditary disease. That this belief, in the same sense as that tubercle may be said to be hereditary, was well founded is quite possible; that is to say, that certain physio-pathological qualities predisposing to the disease may be inherited. But since the discovery of the bacillus it is impossible any longer, if we properly consider it,

to believe that the bacillus itself, and therefore the disease it causes, can be hereditary in the scientific sense of the word "hereditary." Physiological peculiarities and susceptibilities may, but parasites cannot, be inherited. It is true the ovum may be infected by a germ, as in syphilis; but infection is not heredity. That the ovum can be infected at some stage of its existence by the lepra bacillus is proved if it be true that children have been born with the lesions of leprosy on them. But because leprosy is common in the descendants and blood collaterals of lepers, this is no proof of ovum infection in every, or, perhaps, in any case; for family liability is quite as explicable by an hypothesis of contagion or outside infection as by an hypothesis of inherited infection. Not only may the individuals of a family inherit a family predisposition of susceptibility to the bacillus, but, as a family, the members of it are generally at one time or another closely associated, exposed to the same hygienic influences, liable to communicate by contact with each other each other's parasites, or to acquire the parasites latent in their common surroundings. Because the members of a family simultaneously, or one after another, contract scabies, or ringworm, or typhoid, no one supposes on this account that any of these diseases is hereditary.

Without absolutely denying the possibility of ovum infection, the probability is that such an event is very rare. The age at which leprosy usually appears is against such a supposition. The latency of a germ for twenty, thirty, forty, or even seventy years is an extremely improbable thing and without parallel in pathology. Atavism, or, rather, the appearance of atavism, frequently met with in leprosy, is also against such a supposition; for, although we can understand infection of an ovum by a leper parent, we cannot understand the transmission of a germ from a grandparent to a grandchild through a parent who is not, never was, and who may never become, a leper. Such a thing would imply

proliferation of the bacillus in the parent without pathological evidence of its presence.

Even admitting that leprosy is sometimes transmitted by ovum infection, this method of transmission cannot be the only one, or even a common one, for many lepers have no leper ancestors; and, as is well known, the healthy European, coming from a country in which leprosy has not been seen for generations, may acquire leprosy on visiting a country in which the disease is endemic.

If leprosy be communicated generally, or even sometimes, by parent to child by heredity, how explain the striking fact, brought out by Hansen, that of the numerous offspring of 160 Norwegian lepers who emigrated to America not one has become a leper? Or, again, the equally well attested fact that children sometimes become lepers first, their parents afterwards?

Another powerful argument against the doctrine of heredity is the circumstance that lepers become sterile early in the disease. From this it is evident that unless the ranks of leprosy are recruited in some other way than by heredity the disease would inevitably die out in one, or at most, two generations.

From considerations such as these the view that leprosy is a hereditary disease has now few adherents among the well informed.

Contagion. — The best authorities believe that leprosy is propagated by contagion and only by contagion. The same unanimity of opinion does not obtain as to the particular way in which, or medium by which, the contagium is applied; but that it passes directly or indirectly from the infecting leper to the infected, nearly all are agreed to regard as being practically proved. The principal facts and considerations on which this important conclusion is founded are as follows:—

Leprosy is a germ disease, and therefore it cannot originate *de novo*. It must come from a pre-existing germ whose habitat may be air, soil, water, plant,

beast, food, or man. That the habitat of the infecting germ is man is rendered in the highest degree probable by the fact that the germ is found in the human tissues and hitherto nowhere else; and by the fact that leprosy has never been known to appear on virgin soil independently of the prior advent of a leper. When a leper settles down in virgin country, after a time cases of the disease crop up among his companions and immediate neighbours. Some of these new-made lepers, proceeding to a different part of the country, in time become centres for other groups of cases. Thus in the early history of the introduction of leprosy into a virgin country—as New Caledonia—the spread of the disease from individual to individual, and from place to place, can be, and has been traced.

In further proof it can be advanced that not only may a native of a non-leper country acquire the disease on visiting a leper country, but he may also communicate the disease to others, his countrymen, on his return to his own country. There is at least one well-authenticated example of this on record. Dr. Hawtrey Benson, in 1872, showed at the Medical Society of Dublin a leper, an Irishman, who had acquired his disease in the West Indies. After his return to Ireland he slept in the same bed as his brother, who, moreover, sometimes wore the leper's clothes. In time the brother, who had never been out of the United Kingdom, became a leper and was shown to the same medical society in 1877. In this case there can be no question of fact or of diagnosis. Such a case can only be explained by contagion. Many similar, though not quite so well authenticated and conclusive, instances of the communication of leprosy by contagion are on record; but the case just mentioned is alone almost conclusive, for if leprosy is proved to be communicable by contagion in one case, the probabilities are that it is so acquired in every case.

It has been advanced against the contagiousness of leprosy, that it attacks a very small proportion

only of the attendants, nurses, and doctors in leper asylums. But might not a similar objection be raised to the contagiousness of scabies or of ringworm? The conditions for successful contagion are known and can be easily avoided in the latter diseases; they are not known, and are therefore not invariably avoided in leprosy. All contagious diseases demand certain conditions for their diffusion. In some diseases these conditions are easily complied with and often concur; in other diseases they are with difficulty complied with and rarely concur. Leprosy belongs to the latter category.

Probably intimate personal contact, and certain concurrences in the phases of the disease with special conditions in the health or physiological state of the recipient—conditions which are as yet unknown, and which, for all we know, may concur only at long intervals in the intercourse of any two individuals—are necessary for the successful communication and acquisition of leprosy. The simple implantation of the bacillus does not suffice; for, as already pointed out, of the many inoculations that have been made only one has any claim to be regarded as having been successful.

Articles of diet—such as fish—have been incriminated as media for infection. The data on which it is sought to establish this and similar speculations are altogether insufficient, and do not bear investigation.

Prevention.—If it be conceded that leprosy is caused by a germ, that it is contagious directly or indirectly, that it never breaks fresh ground unless first introduced from without and by a leper, then the leper must be regarded as a source of danger, and, *quâ* leprosy, the only source of danger to any community he may live amongst; and that a sure, and the most effectual way of suppressing the disease is the thorough isolation of existing lepers. There are many difficulties, however, in such countries as India, in giving practical expression to what appears to be a

perfectly logical conclusion—difficulties springing from the rights of the individual, finance difficulties, difficulties arising from concealment or incorrect diagnosis, as well as from the continued introduction of fresh cases from without. These and other obvious obstacles, incident to any attempt at a wholesale system of thorough isolation, are so great that the most that can be hoped for at the present time, and in the present state of public opinion, is some modified system of segregation and isolation, such as has worked so successfully in recent years in Norway.

Where possible, therefore, lepers should be segregated in isolated asylums which should be so conducted as to prove attractive. Those who cannot be made, or persuaded, to enter these asylums should be isolated as much as possible from their families and the public; scrupulous cleanliness of their persons and houses should also be insisted on. Lepers ought not to be allowed to beg in the streets as is often the case in Eastern cities, to keep shops, or to handle food or clothes intended for sale, to wander about the country as pedlars or mendicants, to hire themselves out as servants or prostitutes, or to frequent fairs and public places. All lepers in the ulcerative stage of the disease, when it is to be presumed that myriads of bacilli are being constantly given off from their sores, should be still more scrupulously isolated, their discharges, clothes, and dressings being systematically destroyed or disinfected. A child born of a leper should at once be removed from the diseased parent, and, if necessary, cared for at the public expense.

If laws were enacted to give effect to such common-sense precautions, and if these laws were faithfully carried out, the best results might be looked for. Leprosy is feebly contagious, or rather, the conditions for successful contagion rarely recur; so rarely, that it is more than probable that under such a modified system of segregation and isolation as that indicated, they would recur so seldom that the disease would rapidly die out.

Vaccination.—It has not been actually proved that leprosy can be communicated by vaccination, although there is some evidence in favour of such a supposition. But, although this has not been proved, it is an obvious and very desirable precaution in countries in which the disease is endemic to take care that the vaccinifer is not only not the subject of actual leprous eruption, but, also, that he or she comes from a family and community free from leprosy. An apparently healthy vaccinifer may contain lepra bacilli in a latent state, be a potential leper, in fact, capable of communicating the disease.

Treatment.—Scrupulous and systematic attention to personal and domestic hygiene and cleanliness; frequent bathing and the free use of soap; frequent changes of underclothing; good food; fresh air; light work; the avoidance of over-strain, fatigue, and of exposure to bad weather; these things are all of prime importance in the treatment of leprosy, and should be insisted on. It has been found that most lepers on being placed in favourable hygienic conditions improve, at all events for a time, and that in a small proportion the disease by these means may sometimes be actually arrested. Europeans, who have contracted leprosy in the tropics, almost invariably undergo temporary improvement on return to the more bracing climate and more nutritious diet of their native lands.

Many drugs have been regarded, from time to time, as being more or less of the nature of specifics in the treatment of leprosy. But, though some of these drugs appear for a time to do good, and in consequence acquire a certain degree of popularity, hitherto all of them, one after another, have sooner or later fallen into disfavour. There is no good reason to think that any known medicinal substance is really a specific for leprosy, in anything approaching the sense that mercury and iodide of potassium are specific in syphilis. One is very apt to be deceived in estimating the value of a drug in leprosy.

The leper applies for treatment generally during, or soon after, one of the periodical exacerbations of the disease, and when the nodules and other eruptions are active and well pronounced. In the natural course of events, and without treatment of any description, especially if the patient be placed under favourable hygienic conditions, these acute manifestations tend to become quiescent, and the disease temporarily to ameliorate. Observers are too apt to attribute this natural and temporary amelioration to whatever drug the patient may happen to be taking at the time. Moreover, in judging of the value of any drug in leprosy, it must be remembered that the disease may be arrested spontaneously, or even be recovered from, and that without the use of any drug whatever.

Chaulmoogra oil, in doses of from two to ten up to forty drops or more, according to tolerance, three times a day, together with inunction of the same drug mixed with some oil, is a favourite remedy with English practitioners. Gurjun oil, once in favour, seems to have been abandoned.

Unna claims to have cured several cases by the internal administration of ichthyol in increasing doses, combining the internal medication with vigorous rubbing of the arms and legs twice a day with pyrogallic acid (10 per cent.) in lanolin, and the cheeks and trunk with chrysophanic acid (10 per cent.) in lanolin; at the same time applying to the forehead and chin a plaster of chrysophanic and salicylic acids with creasote, changing the plaster every day. The treatment is continued for a month, and is then followed by a course of warm baths before being resumed.

Tuberculin has also been tried. It produces a local and a general reaction, which is sometimes curiously delayed for one or two days. So far from doing good it seems to aggravate the disease, causing fresh eruptions, and, also, causing bacilli to appear in the blood.

Dr. Radcliffe Crocker has recorded (*Lancet*, August 8th, 1896) two cases of leprosy in which great improvement followed weekly hypodermic injections of one-fifth of a grain of perchloride of mercury.

Iodide of potassium aggravates leprosy if given in full doses; it not only affects the general health prejudicially, but it causes fresh eruptions to appear.

Danielssen regards salicylate of soda, combined with cod-liver oil, quinine and iron, good food, and good hygiene, as the best treatment for leprosy. He claims for the salicylate, if commenced within the first few months from the appearance of the disease, that it sometimes effects a cure. He begins with fifteen grains, four times a day, and gradually increases the dose during six months or a year.

I have lately tried thyroidin in a case of nerve leprosy. The patient has improved marvellously since taking it during three years.

Hydroxylamin, europhen, naphthol, salol, methylene blue, and aristol have also been tried recently; the results have not proved encouraging.

Nerve stretching, with or without nerve splitting, has been strongly advocated (McLeod) for the cure of leprous neuralgia, anæsthesia, muscular atrophy, and other trophic lesions. At the best they can benefit the local lesion alone, and that but temporarily, and only in the earlier stages of the leprous neuritis before the nerve has undergone fibrous transformation.

In the case of leprous nodules spreading on to the cornea and threatening to interfere with the line of vision, Broeckmann has shown that the extension of the leproma may be arrested by division of the cornea on the pupillary side of the lesion; it is found that the bacilli do not traverse the cicatrix. Tarsorhaphy for ectropion of the lower lid; iridectomy for iritis, or synechiæ; tracheotomy for laryngeal stenosis; and necrotomy for bone disease, may sometimes have to be performed. The existence of leprosy does not materially interfere with the success of surgical

operations. I once removed an enormous elephantiasis of the scrotum from a confirmed leper; the presence of the leprosy did not prevent sound healing of the extensive operation wound, the man making a good recovery so far as the operation was concerned.

If only one tubercle, or one limited lepra macula is present, and there have been no constitutional signs of a general invasion, it is advisable to excise freely the affected spot. It is just possible that in this spot we may be dealing with the primary lesion of leprosy—the point of invasion—and that as yet the disease is limited to this. At all events, to excise this can do no harm; and in face of the terrible fate which is otherwise in store for the victim of this infection, it would be wrong to withhold any possible chance of escape, however small, such a trifling operation might afford. A case has been recorded (*Arch. de Méd. expér.*, 1st Jan., 1895) in which a child, twenty-seven months old, presented on one temple a minute, red, anæsthetic spot which, on microscopic examination, proved to contain lepra bacilli. The child's brother was a confirmed leper. Six months after the discovery of the spot it was excised and the wound cauterised. This was done in October, 1893; in April, 1894, the child showed no signs of leprosy.

As already mentioned, the occurrence of acute disease may cause absorption of leprous deposit. This has been more particularly observed after erysipelas. It has accordingly been proposed to treat leprosy by inoculations of the erysipelas streptococcus, or by injections of the filtered toxin obtained from cultures of that organism (Impey).

CHAPTER XXVII.

YAWS (FRAMBŒSIA).

Definition.—Yaws—a word of very uncertain etymology -is the name usually employed in English to designate a certain contagious, inoculable disease characterised by an indefinite incubation period, followed usually by fever, by rheumatic-like pains, and by the appearance of a papular rash which usually develops into a fungating, granulomatous, encrusted eruption. It runs a chronic course; is mostly protective against a second attack; and, to a certain extent, is influenced by mercury and potassium iodide

Geographical distribution.—Yaws is widely diffused throughout the greater part of the tropical world. In certain places it is very common as in tropical Africa, particularly on the west coast; in many of the West India islands; in Ceylon, where it is one of perhaps several obscure diseases included under the term *parangi*, in Fiji, where it is known as *coko*; in Java; in Samoa; and in many of the islands of the South Pacific It is difficult to say to what extent it exists in India; some deny its presence there altogether, but recent observations show that it does occur there to a limited extent. Mr. Arthur Powell (*Ind Med. Gaz.*, Sept., 1894, the *Brit Jour. of Dermat.*, No. 98, Dec., 1896) has recognised and described it as occurring in Assam. Possibly some of the skin diseases of the Eastern peninsula, as that described by Dr. W. C. Brown (*Brit. Jour. of Dermat.*, No. 56, Vol v.), under the name of *purru*, as being common in parts of the Malay peninsula, are of this nature. If it occurs in China, it is certainly rare there at all events on the coast. In some of the

West India islands, and in Fiji, almost every child passes through an attack. In the latter, according to Dr. Daniels, those children who do not acquire the disease in the ordinary way are inoculated with it by their parents, who regard an attack of yaws as an occurrence more or less necessary and sanitary. Dr. Nicholls (*Report on Yaws*, Blue Book, 1894) has made a careful and admirable study of West Indian yaws. His inclination is to look upon parangi, coko, and similar Asiatic and Pacific island diseases as specifically different from the African and West Indian disease. Dr. Daniels, however—a most accurate observer, who has had extensive experience both in Fiji and in British Guiana—shows very clearly that in both places the diseases are identical. Probably the view that certain forms of the parangi of Ceylon are not yaws is likewise incorrect.

It is impossible at the present day to settle the point, but it seems probable that yaws was originally an African disease, and, so far as America and the West Indies are concerned, that it was introduced by negro slaves. In the days of West Indian slavery the specific and infectious nature of yaws was thoroughly recognised. The planters from commercial, apart from other, considerations, by instituting yaws houses and other repressive measures, took much trouble to keep the disease under. Since emancipation has permitted the West Indian negro to revert to some extent to the state of savagery from which he had partly emerged, yaws has again become very prevalent, and is now a principal and loathsome feature in the morbidity of these islands

Symptoms.—*The initial fever.*—In yaws there is an incubation stage of very variable duration—two weeks to six months* the appearance of the charac-

* Paulet, who inoculated fourteen healthy persons with yaws, found the first lesion in from twelve to twenty days; Charlouis, in twenty-eight inoculations in thirty-two individuals, observed a papule at the site of inoculation after fourteen days. Naturally acquired yaws seems to have a longer incubation period than the inoculated disease

teristic eruptions being preceded by a certain amount of constitutional disturbance. The intensity of the general symptoms varies within wide limits. Sometimes they are hardly perceptible, and are not complained of; usually there is well-marked malaise with rheumatic pains. Occasionally there is severe constitutional disturbance, lasting for about a week, with rigor, smart fever—100° to 103°—persistent headache, pains—worst at night—in the long bones, joints and loins, and sometimes gastric disturbance and diarrhœa. During the decline of these constitutional symptoms the eruption appears.

Stage of furfuraceous desquamation.—The skin becomes harsh and dry, loses its natural gloss, and here and there patches of light-coloured, very fine furfuraceous desquamation, best appreciated with the aid of a lens, are formed. These patches are usually small and circular; occasionally they are oval, irregular, or form rings encircling islets of healthy skin. Their extent and number are very uncertain. They are mostly scattered irregularly over limbs and trunk; but occasionally they may be almost confluent, the patches coalescing and giving rise to an appearance as if the entire skin had been dusted over with flour. On the other hand, this furfuraceous desquamation may be so slight as to be overlooked. In other instances it may be very marked; the heaping up of desquamating epidermic scales producing white marks, very evident on the dark skin of a negro or Oriental.

This patchy, furfuraceous condition of the skin occurs not only at the early stage of yaws, but it may persist throughout the attack, or reappear as a fresh eruption at any period of the disease.

The yaw.—When the furfuraceous patches have been in existence for a few days minute papules appear in them. Describing these papules, Dr. Nicholls remarks that, in examining them with a lens, "they are seen to be apparently pushed up from the rete malpighii through the horny epidermis, which breaks

over their summits and splits in lines radiating from the centre, the necrosed segments curling away from the increasing papule. When the papules become about a millimetre in height and breadth, a yellow point may be observed on the summits . . . . . consisting not of a drop of pus under the epidermis . . . but of a naked, cheesy-looking substance, which cannot be wiped away unless undue force be used. Frequently a hair will be observed issuing from this yellow substance, thereby indicating that the hair follicles are the centres of the change going on." This eruption may persist during the entire attack, or it may appear at any time during the course of the disease. When extensive and occurring late, it indicates a protracted attack

The papule, having arrived at this stage, may either cease to grow, the apex becoming depressed, cupped, and lined with the yellow cheesy material alluded to, or it may go on, increasing in size, to the formation of the typical yaw In the latter case the lesion gradually grows into a rounded excrescence, the yellow material at the top widening out so as to form a complete cap encrusting the little tumour. The yaw so formed may be no larger than a split pea; or it may attain the breadth of a crown piece. The smaller tumours are hemispherical; the larger are more flattened or even depressed at the centre, possessing everted, somewhat overhanging, rounded edges. Occasionally, though rarely, a big yaw may include an area of sound skin. Several yaws may coalesce, and together cover a large and irregular surface, as an entire cheek, a popliteal space, or the dorsum of a foot. In the case of these large yaws, the surface of the growth is apt to be irregular and fissured. The neighbourhood of the mouth and anus are favourable sites for coalescent yaws; in such situations the moisture of the parts softens and removes the crust wholly or in part, so that the surface, in addition to being fissured, may be more or less bare, sodden, and fungoid.

The crust which caps and encloses an uninjured yaw is yellowish, granular, blotched with blood stains and encrusted dirt. At first the crust is somewhat moist, but gradually it becomes dry, brown, and black even. The crusts are firmly adherent, requiring some force to remove them; a proceeding which, though painless, may entail a little oozing of blood. Deprived of its crust, the little swelling is seen to be red in colour, and generally smooth and rounded on the surface. According to size, it stands out anything from one-eighth to six eighths of an inch above the surrounding healthy skin. Immediately after removal of the crust, the exposed surface begins to pour out a pale, yellowish-grey, viscid fluid, which soon becomes inspissated, rapidly forming a fresh cap to the yaw. Pus, unless as a consequence of irritation, is not, as a rule, found under the crust.

Although the formation of the papules and yaws is attended with much itching, the yaw itself is not at all sensative. Tearing off the crust therefore, as stated, gives no pain; the tumour may be touched with acid even with impunity—a diagnostic point of some importance.

The yaw usually attains its maximum development in two weeks; for several weeks longer it remains stationary, and then begins to shrink. The crust then thins, shrinks, darkens, separates at the periphery, and at last falls off, disclosing at the site of the former fungating mass a slightly thickened (pale—Nicholls, hyperpigmented—Daniels) spot of fairly sound skin.

Ulceration. Such is the normal process of evolution and involution of a yaw. But it sometimes happens that the tumours, in place of becoming absorbed, break down and ulcerate, the ulceration, however, being confined to the yaw itself. In other instances ulceration goes deeper and extends laterally, giving rise to extensive sores with subsequent cicatricial contractions. Such ulcerations may or may not be encrusted. With the development of the

deeper and wider forms of ulceration, the typical lesions of yaws may disappear for a time, or perhaps permanently. In the latter case the ulcers are said not to be infective, and do not communicate yaws; they are, therefore, to be regarded rather as complications or, it may be, sequelæ. Such ulcers may persist for years. Ulceration, according to Dr. Nicholls, occurs in about 8 per cent. of cases.

Onychia.—Yaws may occur around or under a nail and give rise to a troublesome form of onychia.

Foot yaws.—When a yaw develops on the sole of a foot, in consequence of being bound down by the dense and thick epidermis, it causes much suffering. Spreading laterally under the thick, leathery, and unyielding epidermis, it may attain a large size. After a time, however, the epidermis over the growth gives way, splitting in a radiating fashion; pressure being thus removed the yaw fungates, and, at the same time, suffering diminishes.

A cracked scaly condition of the hands and feet, sometimes persisting for years, is not unusual in negroes and must not be confounded with yaws, although not infrequently the two conditions co-exist.*

Distribution.—The tumours may be scattered over

* In the course of time the West Indian negroes have adopted a peculiar jargon—a mixture of French, English, and Spanish—to designate the various manifestations of yaws. The scaly patches are known in some of the islands as "pian dartres," in Jamaica as "yaws cacca"; the papular stage of eruption as "pian gratelle"; when the papular eruption occurs as a late symptom, it may be called "pian charaib," or "guinea-corn yaws." The developed yaw is sometimes known as "bouton pian." "Tubboes," "tubba," "crabs," "crappox," "crabes," are expressions applied to the painful manifestations on the soles of the feet. Forms of chronic dermatitis on hands and feet are called "dartres," "tubboe," "crabs," "dry tubboes"; or where exudation goes on between cracks in soles or palms, "running crab yaws." A large persistent yaw is sometimes known as the "mother," or "grandmother," or "mama-pian"; smaller yaws as "daughter" or "grand-daughter" yaws. Yaws which show themselves some time after the disease appears to have subsided are called "memba" (remember) yaws. Yaws coalescing in the form of a ring are called "ringworm" yaws.

the whole body; or the crop may be limited to one or two growths; or they may be confined to a circumscribed region of the skin. They are commonest on exposed parts, on the anterior surface of the body, and on parts much exposed to injury, as the feet and legs. They are most frequently found on the lower extremities; rarely on the scalp, and still more rarely in the axillæ. They are hardly ever seen on mucous surfaces unless about the lips, around the angles of the mouth, and in the nostrils, where they often form clusters.

Duration and recurrences.—Yaws lasts for weeks, months or years, its duration depending on the general health, on idiosyncrasy, hygienic conditions, and the treatment employed. Mild cases in healthy subjects finish in about six weeks. In other instances, especially in the debilitated, the disease runs on for months, successive crops of eruption being evolved. Sometimes these recurrences may stop short at the stage of desquamation, or at the papular stage, or they may proceed to the formation of typical yaws. The recurrences are usually preceded by feverishness, pains in the bones and joints; and the successive crops may either be limited and partial in their distribution, or they may be general. In Fiji, Daniels states, the average duration of an attack of yaws is about one year.

The general health.—With the exception of during the initial fever, or during one of the recurring febrile relapses, the general health is not as a rule affected. Occasionally there is debility and cachexia; or there may be enlargement and tenderness of the lymphatic glands. In other instances the rheumatic pains are a principal feature and may be very severe.

Persistent yaws.—That yaws sometimes effects a permanent hold is shown by the persistency with which they occasionally continue to recur during many years. In such cases the lesion has always the characters of a true yaw, and cannot be regarded as a "secondary" or "tertiary" manifestation in the sense

in which these terms are applied to the late lesions of syphilis.

Question of sequelæ.—Mention is often made of nodes, of gummatous-like thickenings, and of punched out and serpiginous ulcerations in connection with yaws. Most recent authorities, however, regard all such phenomena as essentially the results of an independent, though concurrent, syphilitic infection.

It sometimes happens that an individual who years previously passed through an attack of yaws is affected with destructive ulceration of the soft palate, or of the mucous membrane and cartilage of the nose. Opinions differ as to the true relationship between this ulceration and the antecedent yaws; some holding that it is a later manifestation of yaws, others regarding it as purely the result of an independent syphilitic taint. As regards the West Indies the question is one which, considering the great frequency of both acquired and congenital syphilis there, it is hard to decide. Daniels, however, says that in Fiji, where syphilis is unknown among the natives these destructive ulcerations of palate and nose, together with a skin affection like lupus vulgaris—all of which he says are amenable to potassium iodide—are not uncommon; he is inclined, therefore, to regard them as true sequelæ of yaws.

Question of a primary sore.—Another point in the symptomatology of yaws is the question of the occurrence of a primary sore, as in syphilis. Numa Rat says there is such a sore, but that it is usually overlooked. He describes it as a papule with a pale yellow material at its apex, which may remain a papule, or which, after seven days, may ulcerate and subsequently cicatrise. Other observers do not agree with this. They say that though yaws virus applied to a pre-existing ulcer may render it unhealthy-looking and cause it to fungate like an ordinary yaw, yet successful puncture inoculations, although they sometimes give rise to a yaw at the point of inoculation, do not by any means always produce a local lesion,

much less an ulcer. The lower animals appear not to be susceptible to yaws; this, and other interesting points, therefore, cannot be settled by experiment on them

Mortality.—Although in the literature of the subject reference is made to deaths from yaws, yet, judging from the statistics collected by Nicholls, the mortality must be very small indeed. In 7,157 West Indian cases, treated in various yaws hospitals, there were only 185 deaths—a mortality of 25·8 per thousand, a death rate, as Nicholls points out, less than the average annual death-rate in one of the islands —Antigua. Doubtless, however, although yaws itself rarely directly proves fatal, intercurrent diseases, such as sloughing phagedæna and phagedænic ulceration, predisposed to by the skin lesions, occasionally do so. If the verruga of Peru be yaws, then, under certain conditions, yaws becomes a very dangerous disease.

Ætiology.—*Contagion and heredity.* As yaws is highly contagious, all circumstances favouring contact with the subject of the disease favour its occurrence. Simple skin contact does not suffice for infection; a breach of surface is necessary. Probably the virus is often conveyed by insect bites, or by insects acting as go-betweens and carrying it from a yaws sore to an ordinary ulcer. Thus the disease often commences in a pre-existing ulcer. Cases are prone to originate in certain dirty houses, the virus from previous yaws patients seemingly impregnating the floors and walls of the filthy huts in which the latter had resided. In this way the disease may be acquired without direct transference from an existing case. Yaws is neither hereditary nor congenital. A pregnant mother suffering from yaws does not give birth to a child suffering from the same disease; or one which will subsequently develop yaws, unless the virus be introduced after birth directly through a breach of surface. It is not conveyed by the milk; nor does a suckling suffering from yaws necessarily infect its nurse.

Age, Sex, Occupation, Race.—Although two-thirds of the cases in the West Indies occur before puberty, no age is exempt. Three males are infected to every female attacked. Occupation has no manifest influence. In the West Indies, Europeans, Chinese, and Indians catch the disease if exposed to the contagion.

Morbid anatomy and pathology.—No visceral changes have been found in yaws, although, of course, when yaws concurs with syphilis, gummata, etc., may be found; but in this case the concurrent gummata belong to the syphilitic and not to the yaws infection.

The tumours on the skin are granulomata made up of round or spindle-shaped cells, held together by a small amount of connective tissue and abundant blood-vessels. The focus of the circumscribed cell proliferation is the papillæ which become very much swollen, and the malpighian layer. The cause of the proliferation is probably some micro-organism; what this may be has not been satisfactorily determined. Both Pierez and Nicholls found a micrococcus in great profusion in the growth and exudation. This they succeeded in cultivating; but the causal relationship of the bacterium to the disease has not been established, inoculations of cultures into the lower animals proving negative.

Diagnosis.—A painless, insensitive, larger or smaller, circular, encrusted, red granulomatous excrescence, occurring in the endemic district, is almost certainly yaws. The most important point in connection with yaws, both as regards diagnosis and ætiology, is its relationship to syphilis. It has been, and is still, held by some distinguished authorities, Hutchinson for example, that yaws is possibly syphilis modified by race and climate; and certain features which the two diseases have in common are pointed to in support of the contention. The discussion is bound to continue until the respective germs of yaws and syphilis have been separated, cultivated, and inoculated. So far as clinical and

microscopical evidence goes, it is decidedly in favour of, not to say conclusive for, regarding the two diseases as specifically distinct. There are many points of contrast in their clinical features. I may mention the primary sore, the infection of the fœtus, the adenitis, the exanthem, the alopecia, the absence of itching, the iritis, the affection of the permanent teeth, the bone and eye affections, the congenital lesions, the polymorphism of the eruptions, the nerve lesions and the gummata of syphilis. All these are wanting in yaws. Moreover, both diseases may concur in the same individual (Powell cites two cases, and Charlouis two, of syphilis supervening on yaws); and antecedent syphilis certainly does not confer immunity as against yaws. Yaws may die out in a community, as in British Guiana (Daniels, *Brit. Jour. of Dermat.*, November, 1896), yet syphilis remain; yaws may be universal in a community, as in Fiji, and yet true syphilis, whether as an acquired or congenital disease, be unknown. Finally, syphilis has never been shown to give rise to yaws, nor yaws to syphilis; neither, so far as known, has yaws been evolved in any community from syphilis, or appeared independently where the possibility of its having been introduced from a recognised yaws centre could be excluded with certainty.

The therapeutical argument for the identity of the two diseases is a very fallacious one. Sulphur will cure scabies and pityriasis versicolor; yet from this circumstance we may not conclude that these diseases are identical. The same may be said in respect of the influence of mercury and iodine on syphilis and on yaws.

Prophylaxis.—This resolves itself into the adoption of measures to prevent contagion. These are, the isolation and segregation of the affected; the dressing and treating of wounds in the hitherto unaffected; the application of antiseptic ointments to yaws sores so as to obviate the diffusion of germs; the purifying or destruction by fire of houses or huts notoriously

infected; the prevention of pollution of bathing water by yaws discharges.

Treatment.—All are agreed as to the propriety of endeavouring by good food, tonics, and occasional aperients to improve the general health. Most are agreed as to the propriety of endeavouring to procure a copious eruption by stimulating the functions of the skin by warm demulcent drinks; by a daily warm bath with plenty of soap; and, during the outcoming of the eruption, by such diaphoretics as liquor ammoniæ acetatis, guaiacum, etc. Confection of sulphur is also recommended as a suitable aperient; it may be taken frequently in the early stages of the disease. All are agreed as to the propriety of avoiding everything—such as chill—tending to repress the eruption; warm clothing is therefore indicated. Many use mercury or potassium iodide, or both, after the eruption is fully developed. These drugs have undoubtedly the power of causing the eruption in yaws to resolve. Some practitioners rarely use them or, if they use them, do so only at the latest stages of the disease, considering that relapses are more prone to occur after their too early employment. Mercury, owing to its proneness to cause anæmia, is less frequently employed than potassium iodide. Where the eruption is persistently squamous, or papular, arsenic is frequently prescribed. Some touch the yaws with sulphate of copper: some apply nitrate of mercury ointment: others iodoform ointment: others leave them alone, confining their local measures to the enforcement of cleanliness. When the soles of the feet are attacked, the feet ought to be soaked in warm water to soften the epidermis, which should then be cut away sufficiently to liberate the subjacent yaw. Ulceration must be treated on ordinary principles. During convalescence, iron, arsenic, and quinine are indicated.

CHAPTER XXVIII.

VERRUGA PERUANA.

In certain narrow valleys of the Andes, between the ninth and sixteenth parallels of south latitude, and at an elevation of from 3,000 to 10,000 feet, an aggravated form of a disease closely allied or identical with yaws, and locally known as "verruga," is endemic.

The peculiar initial rheumatic-like pains and fever are apparently identical with those of yaws, only they are more severe. Just as in yaws, one attack of verruga confers immunity. The constitutional symptoms, likewise, subside on the appearance of the skin lesion which, judging by the published descriptions, is a granuloma macroscopically and microscopically identical with that of yaws. Just as in the latter disease, the eruption may be sparse or abundant, discrete or confluent. As in yaws, individual granulomata may fail to erupt; others may subside rapidly; others again may continue to increase, and then, after remaining stationary for a time, gradually wither, shrink, and drop off without leaving a scar. If difference there be between verruga and yaws, apparently it is more one of degree than of kind.

In verruga the initial fever may continue for weeks, or even for months. It is very severe in many instances. Often it exhibits features like those of a malarial infection, including intermittency, profound anæmia, and sometimes enlargement of the spleen and liver. Very probably in such cases it is the outcome of a compound infection—verruga attacking a malarial subject. Not infrequently in the endemic district a certain type of fever, believed to be verruga

fever, proves fatal before the appearance of definite skin manifestations such as would justify a positive diagnosis. This was apparently the case with a medical student, hamed Carrion, who inoculated himself with blood from a verruga granuloma. The symptoms in his case closely resembled those of the very deadly fever referred to, which is known locally as Oroya fever.

In addition to the severity of the fever and rheumatic pains, the Peruvian disease is remarkable for the tendency to spontaneous hæmorrhage exhibited by the skin lesions. Apparently this peculiarity is attributable, like the hæmorrhages in the affection known as "mountain fever," to the diminished atmospheric pressure at great altitudes; for when the patients descend to the lower valleys, or to the sea level, the tendency to bleeding ceases. Doubtless, the unusual vascularity of the swellings, which are sometimes permeated by a network of cavernous sinuses, also arises from the same circumstance.

In yaws we find no mention made of the occurrence of fungating granulomata in any situation but the skin. In verruga it would seem that the tumours may develop on mucous surfaces—in the œsophagus, the stomach, intestine, bladder, uterus, and vagina. Hence the dysphagia—a common symptom—and the occasional occurrence of hæmatemesis, melæna, hæmaturia, and bleeding from the vagina in the last-named disease.

The geographical distribution of verruga, so far as known, is singularly limited; it is confined to certain valleys, the inhabitants of neighbouring places being exempt. It is said that the disease may be acquired in merely passing through the endemic districts; and that, unlike yaws, the domestic animals in these districts, as well as the human inhabitants, are subject to the disease.

Treatment.—It appears that cold tends to repress the development of the eruption, and that until this appears fever and pain persist. For this reason

as well as to avoid the hæmorrhage from the lesions when they do erupt, the patients should quit the heights and descend to near the sea level. External hæmorrhages, when they do occur, must be treated by graduated pressure; otherwise, the local as well as the general treatment is the same as in yaws.

CHAPTER XXIX.

ULCERATING GRANULOMA OF THE PUDENDA.

Geographical distribution.—Drs. Neal, Ozzard, Conyers and Daniels (*Brit. Guiana Med. Ann.*, 1896) describe a peculiar form of ulcerating granuloma affecting the pudenda in dark-skinned races. Their observations were made in British Guiana and, principally, on West Indian negroes. Daniels believes that he has seen a similar, or the same disease, in Fijians. If it be the case that this affection occurs in places so far apart as Fiji and Guiana, the probability is that, although hitherto overlooked, it occurs in other tropical countries also.

Age and sex.—This form of groin ulceration has not been observed before puberty; it has been found only after thirteen or fourteen and up to forty or fifty. It occurs in both sexes, but particularly in women.

Symptoms.—The disease commences somewhere on the genitals or groins as an insignificant, circumscribed, nodular thickening and elevation of the skin. The affected area, being covered with a very delicate, pinkish, easily-rubbed-off epithelium, excoriates readily, exposing a surface prone to bleed and break down, although rarely ulcerating deeply. The disease advances in two ways; by continuous eccentric peripheral extension and by auto-infection of an opposing surface. In its extension it exhibits a predilection for warm and moist surfaces; particularly the folds between the scrotum and thighs, the labia, and the flexures of the thighs (Fig. 34). Its extension is very slow, years elapsing before it covers a large area. Concurrently with peripheral extension a dense, contracting, uneven, readily-breaking-down scar forms on the surface travelled over by the coarsely or finely nodulated active

new-growth which constitutes the peripheral part of the diseased area. Occasionally islands of active disease spring up in this scar tissue; but it is at the margin of the implicated patch that the special features of the affection are to be observed. In a case of some standing there is found a large area of white or irregularly pigmented, perhaps excoriated, unsound, contracting,

Fig. 34.—Ulcerating granuloma of the pudenda in the male.

folded, and dense cicatrix, surrounded by a narrow, serpiginous, irregular border of nodulated, somewhat raised, red, glazed, delicately skinned or pinkish, superficially ulcerated or cracked new-growth.

In the case of the female (Fig. 35) the disease may extend into the vagina, over the labia, and along the flexures of the thighs. In the male it may spread over the penis, involve the glans, scrotum, and upper part of the thighs. In either sex it may spread in the course of years to the pubes, over the perineum, and as far back as the region of the coccyx. At times a profuse watery discharge exudes and even drips from the surface of the new-growth, soiling the clothes, soddening the skin, and emitting a peculiarly offensive odour. In this condition the disease, slowly extending,

continues for years, giving rise to inconvenience and perhaps seriously implicating the urethra, vagina, or anus, but not otherwise materially impairing the health.

Histology. On microscopical examination the new growth at the margins of the sore is found to be made up of nodules, or masses of nodules, consisting of round cells having large and, usually,

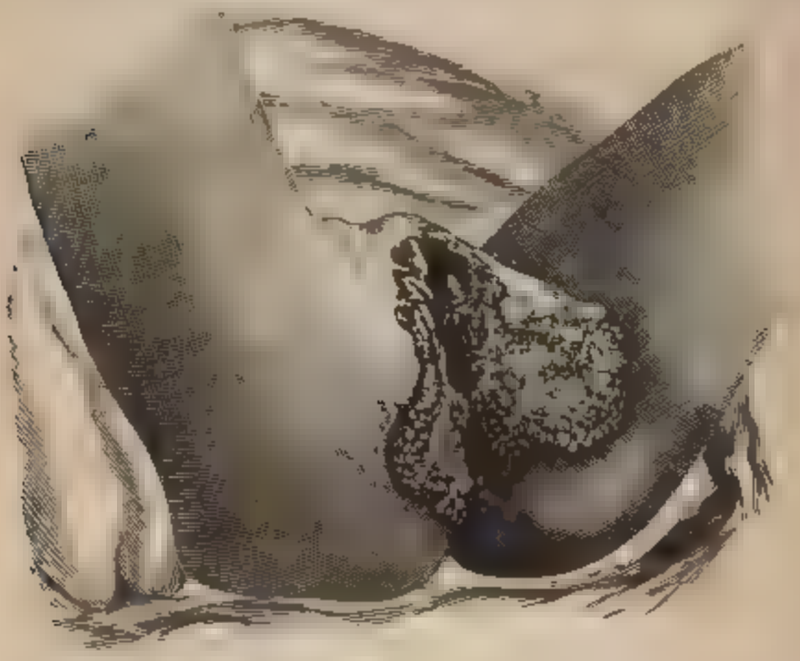

Fig. 46. Ulcerating granuloma of the pudenda in the female.

badly staining nuclei. These cells are imbedded in a delicate fibrous reticulum. The nodular masses are, for the most part, covered by epithelium, their under surfaces merging gradually into a dense fibrous stroma in which small clusters of similar round cells are here and there embedded. The growths, though very vascular, contain no hæmorrhages, and there are no signs of suppuration or of caseation, no giant cells, and no tubercle bacilli. In a section of one of the small nodules the round cell mass will be found to be wedge-shaped, the base of the wedge being towards the skin, the deep-lying apex usually pierced by a hair or two. The growth is found around sebaceous follicles, blood

vessels, lymphatics, and sudoriporous glands; but it is specially abundant, and most deeply situated, around the hair follicles. No characteristic micro-organism has hitherto been discovered. For a detailed description of the histology the reader should consult an elaborate article by Dr. James Galloway, in the *British Journal of Dermatology*, April, 1897.

Diagnosis.—In British Guiana, as elsewhere, malignant and syphilitic ulcerations of the groin are common enough; the disease under notice, however, differs widely from these both clinically, histologically, and therapeutically. It is characterised by extreme chronicity—ten or more years—by absence of cachexia or of any tendency to cause death, by non-implication of the lymphatic system, and by non-amenability to mercury and iodide of potassium. The disease which it most resembles is lupus vulgaris. From this it differs inasmuch as it is practically confined to the pudendal region, affects mucous as well as cutaneous surfaces, tends to follow in its extension the fold of the skin, is not associated with the tubercle bacillus, giant cells, caseation, or other evidences of tuberculous disease.

Treatment.—This disease is very rebellious to treatment. Scraping and caustics, including the actual cautery, have been freely employed; but, although some improvement may be effected by these means, new nodules almost invariably spring up in the resulting cicatrix. Complete excision, where practicable, offers the best chance of permanent cure; of course, such a proceeding must be undertaken before large areas and important passages have become involved. Drs. Conyers and Daniels have found that camphor and carbolic acid in equal parts, and salicylic acid in unguentum creasoti, thirty to forty grains to the ounce, give the best results; although in no instance have they succeeded in effecting a complete cure, the growth invariably recurring in the scars soon after discontinuance of treatment. Mercury and iodide of potassium are useless.

CHAPTER XXX.

ORIENTAL SORE.

Definition. A specific ulcerating granuloma of the skin, endemic within certain limited areas in many warm countries It is characterised by an initial papule which, after scaling and crusting over, breaks down into a slowly extending and very indolent ulcer Healing after many months, it leaves a depressed scar. The sore is inoculable and, to a considerable degree, protective against recurrence.

Geographical and seasonal distribution.—Among the endemic places may be named Morocco, the Sahara (Biskra, Gafsa), Egypt, Crete, Cyprus, Asia Minor, Syria (Aleppo), Mesopotamia (Bagdad), Arabia, Persia, the Caucasus, Turkestan, India (Lahore, Multan, Delhi, etc.). Locally, Oriental sore is often called after some town or district in which it is specially prevalent; thus we have Delhi boil, Bagdad boil, and so forth. It is much more common in cities than in the country In Bagdad few escape an attack; visitors, even of a few days only, are almost certain, at particular times of the year, to contract it. Juliano describes (*Jour. des Mal. Cut. et Syph.*, Oct., 1890) the disease as being common in Bahia, Brazil, the name Oriental sore, suggested by Tilbury Fox, is therefore no longer quite appropriate.

According to Hirsch, in the tropics this form of ulceration is specially prevalent about the commencement of the cool season, in temperate climates towards the end of summer or beginning of autumn Years of prevalence may be succeeded by years of

comparative rarity ; possibly in harmony with altered sanitary conditions. In Delhi, for example, in 1864 from 40 to 70 per cent. of the resident Europeans were affected with the local sore ; on certain sanitary improvements being effected, the frequency of the disease was immediately materially reduced.

Symptoms. — Oriental sore commences as a minute, itching papule which tends to expand somewhat as a shotty, congested infiltration of the derma. After a few days the surface of the papule becomes covered with fine, papery scales. At first these scales are dry and white ; later they are moister, thicker, browner, and adherent. In this way a crust is formed which, on falling off, or on being scratched off, uncovers a shallow ulcer. The sore now slowly extends, discharging a scanty ichorous material which, from time to time, may become inspissated and crust over the sore which continues to spread underneath. The ulcer extends by the erosion of its perpendicular, sharp-cut, and jagged edge, which is surrounded by a slight or more considerable areola of congestion. The surface of the ulcer is irregular. Any granulations which form speedily break down. Subsidiary sores may arise around the parent ulcer, into which they ultimately merge. These sores, usually about an inch or so in diameter, in process of time may come, in some instances, to occupy an area several inches across.

After a variable period, ranging from two, or three to twelve, or even more months, healing sets in. Granulation is slow and frequently interrupted. Often it commences at the centre whilst the ulcer may be still extending at the edge ; often it is effected under a crust. Ultimately a depressed, white, or pinkish cicatrix is formed. Contraction of the scar, particularly if it happens to be on the face, may cause considerable and unsightly deformity.

Oriental sore may be single or multiple. Two or three are not uncommon ; in rare instances as many

as forty have been counted on the same patient. They are mostly situated on uncovered parts hands, feet, arms, legs, and, especially in young children, on the face; rarely on the trunk; never on the palms, soles, or hairy scalp.

In a very few instances the initial papule does not proceed to ulceration but persists as a scaling or scabbing, non-ulcerating, flattened plaque -just as sometimes happens in the case of the primary chancre of syphilis. Occasionally, from contamination with the virus of erysipelas, of sloughing phagedæna, or of some other infectious acute inflammatory skin disease, the primary lesion may become complicated and correspondingly modified and, perhaps, a source of serious danger. Otherwise, Oriental sore is more troublesome and unsightly than painful or dangerous.

Histology; ætiology.—Section of the papule displays an infiltration of the derma by a mass of small round granulation cells. They lie between the elements of the tissues, particularly about blood-vessels, lympathics, and sweat glands; towards the centre of the lesion they completely replace the normal structures. Various micro-organisms have been described in association with Oriental sore. By staining sections in gentian violet and afterwards partly decolorising in spirit, Cunningham and Firth found certain violet-stained bodies, varying in size and grouping, in a proportion of the infiltrating cells. These bodies Cunningham was inclined to regard as parasites. Riehl, however, looks upon them as the result of a hyaline degeneration of protoplasm, and advances a claim for certain micrococci which he found in great profusion in the granulation cells. Other observers have likewise found micrococci in the tissues; but, so far, inoculations from cultures have failed to produce the sores. As the disease has been proved to be communicable to the lower animals (as well as to man) by inoculation of the discharge from the surface of the ulcers, there can be little doubt that in Oriental sore the discharges contain the

specific germ; and, as Riehl's micrococcus did not communicate the true type of sore, it is probable that the germ has yet to be discovered.

In what way, under natural conditions, the parasite enters the tissues it is as yet impossible to state definitely. Not improbably it is conveyed by flies or other biting insects, and by them either inserted into the skin or applied to some pre-existing wound or sore.

As a rule, second attacks do not occur. Observing this, the Jews of Bagdad at one time practised on their young children Oriental sore inoculation, selecting for the purpose some part of the body habitually covered by the clothes. They designedly forestalled the infection by natural agencies, which experience had taught them to regard as inevitable; and thereby avoided an ugly scar on the faces, hands or arms of their children.

Neither race, sex, age, occupation, nor social condition influences susceptibility.

Treatment.—Some have advocated destruction of the primary papule, and even of the ulcer, by caustics or by the actual cautery. It is doubtful if such a measure would prove effective. A knowledge of the nature and natural progress of the disease suggests a protective and soothing, rather than an irritating line of treatment. A dressing with some mild antiseptic ointment, as of iodoform, boracic or salicylic acid, is indicated. Tonics when the patient is anæmic or debilitated, attention to the general health, change of climate should the disease persist beyond the usual time for cicatrisation, are also indicated.

SECTION V. ANIMAL PARASITES AND ASSOCIATED DISEASES.

CHAPTER XXXI.

FILARIASIS.

He who would properly qualify himself for medical work, in warm countries especially, must acquire something more than a smattering of helminthology. The conditions of life in the tropics are such, that not only are the careless natives extremely subject to verminous invasions of many descriptions, but the more carefully living and fastidious European is also constantly exposed to being victimised in the same way. Obscure diseases are very often the expression of some form of helminthiasis, and many diseases which formerly were mysterious and inexplicable can now with confidence be referred to "worms." The ability to recognise the presence of these parasites has, in some instances, enormously enhanced our powers of diagnosis, treatment, and prophylaxis. The physician, therefore, cannot afford any longer to ignore what, not many years ago, was regarded as but an unimportant department of natural history.

I. PARASITES OF THE CIRCULATORY AND LYMPHATIC SYSTEMS.

THE FILARIÆ SANGUINIS AND FILARIASIS.

History. Our knowledge of this subject dates from the discovery by Demarquay, in 1863, of an embryo nematode *filaria nocturna*—in the milky fluid from a case of chylous dropsy of the tunica vaginalis (p. 464). Later, in 1866, Wucherer found the same organism in the urine of a number of cases of

chyluria. In 1870 Lewis made a similar observation in India. Two years later, in 1872, the latter observer discovered that the blood of man was the normal habitat of this embryo parasite which he named, accordingly, *filaria sanguinis hominis*. Since that date the subject has rapidly expanded, and its great practical importance in tropical pathology is now slowly becoming recognised. Recently the writer has pointed out that Lewis's filaria is not the only bloodworm in man, and that the human circulation is the habitat of the embryos of no fewer than four, possibly of five or even more, distinct species of nematodes.

Nomenclature.—In consequence of the discovery of so many additional and similar blood parasites, it has been deemed advisable to modify the original name of Lewis's filaria. This I have proposed to call *filaria nocturna*. The other filariæ of the blood I have named *filaria diurna*, *filaria perstans*, *filaria Demarquaii*, *filaria Ozzardi*, and a sixth, which may or may not be connected with one of the two last, has been called *filaria Magalhãesi*, after its describer.

Their pathological importance.—Only two of these parasites, so far as we know at present, appear to have important pathological bearings—*filaria nocturna*, the embryonic form of *filaria Bancrofti*, a mature parasite inhabiting the lymphatics of man; and *filaria perstans*, probably the embryo of a parasite which has but recently been discovered. The pathological significance of the latter is still doubtful. There can be no question of the importance in tropical pathology of *filaria nocturna* and of its parental form; there is abundant reason to believe that it is the cause of endemic chyluria, of various forms of lymphatic varix, of tropical elephantiasis Arabum, and probably of other obscure tropical diseases.

FILARIA NOCTURNA (*filaria Bancrofti*).

Geographical distribution and prevalence.—The geographical distribution of *filaria noc-*

turna is very extensive. It has been found as an indigenous parasite in almost every country throughout the tropical and subtropical world, as far north as Spain, in Europe, and Charleston, in the United States of America; and as far south as Brisbane, in Australia. In many places quite 10 per cent., and in other places half, of the population harbour it. I have ascertained that it is probable that one-third of the inhabitants of at least one district in India—Cochin—carry blood filariæ. I also find that in some of the South Sea islands, Samoa, for example, fully one-half of the people are affected in this way. Thorpe has shown (*Brit. Med. Jour.*, Oct. 3rd, 1896) that in the Friendly Islands 32 per cent. of the people harbour the filaria. The table on p. 449, drawn up from a number of observations on the blood of the natives of certain tropical countries, will convey some idea of the wide area over which this and the other blood filariæ are distributed, and of the degree of their prevalence in the countries mentioned.

Demonstration of blood filariæ.—Whoever would investigate the subject of filariasis will find that, in order practically to comprehend the subject and provide himself with abundant material for observation, it is advisable to make a systematic examination of the blood of the inhabitants of some district in which elephantiasis is endemic. If this be done, the observer is sure to come across, sooner or later, cases in which *filaria nocturna* abounds, and also of the diseases to which it gives rise.

I commend the following procedure as likely to supply the investigator not only with material but, also, with much useful information. Let him visit *late in the evening* some hospital or prison, or other establishment where he can have an opportunity of examining the inmates, and let him procure slides of the blood of, say, 100 individuals. The slides are conveniently prepared by pricking the finger of each individual in turn, transferring large drops of the blood so obtained to ordinary microscope slips by

Region	Locality.	No. of Cases examined.	Day or night blood.	Filaria nocturna.	Filaria diurna.	Filaria Demarquaii.	Filaria perstans.	Filaria Ozzardi.
West Africa	Congo, Dr. Firket	54	D	—	—	—	30	—
	Lukunga (Congo)	14		—	—	—	9	—
	Banza Manteka (Congo)	61		—	—	—	35	—
	Old Calabar	27		1	1	—	15	—
	Lower Niger	108	Both	8	16	—	3	—
	Dahomey	49	Both	2	—	—	1	—
East Africa	Zanzibar	1	—	1	—	—	—	—
	Mombasa	40	—	1	—	—	—	—
	South-East Africa	74	—	—	—	—	—	—
North Africa	Morocco	6	5 p.m.	—	—	—	—	—
India	Madras	6	—	1	—	—	—	—
	Cochin	88	Night	21	—	—	—	—
Ceylon	Ceylon	56	Both	1	—	—	—	—
South Pacific	Samoa	56	Night	27	—	—	—	—
	Fiji (Dr. Thorpe)	124	Both	30	—	—	—	—
	Friendly Islands (Dr. Thorpe)	214	Both	69	—	—	—	—
British Guiana	Georgetown, Dr. Daniels	348	Night	52	—	—	—	—
	New Amsterdam, Dr. Ozzard	100		28	—	—	—	—
	Demerara Indians „ „	72	—	—	—	—	—	45
	„ „ Dr. Daniels	99	—	—	—	—	—	55
	Demerara littoral	61	Night	9	—	—	—	—
West Indies	St. Vincent	152	Both	6	—	10	—	—
	St. Kitts and Mont Serrat	28	Both	6	—	—	—	—
	Trinidad	70	Both	6	—	—	—	—
	St. Lucia	72	Night	—	—	4	—	—

simply dabbing the centre of the slip on the blood. The blood is then spread out with a needle, so as to cover in a moderately thin film about a square inch of one surface of each slip. The slips are allowed to dry; they are then labelled and put aside. One preparation of this description may be made from each individual, who should be selected simply as a representative of the general population, and therefore irrespective of his being physically sound, or of his being the subject of any particular type of disease.

The slides may be examined in various ways, either at once or, if more convenient, weeks or months afterwards; if kept dry, they do not spoil. A convenient plan is to dip the slides, without previous fixing, in a weak solution of fuchsine—about three or four drops of the saturated alcoholic solution to the ounce of water. They are left in the stain for about an hour, and then examined wet and without cover-glass. If the slides are old, they may stain too deeply; in this case they may be partially decolourised in weak acetic acid—two or three drops to the ounce of water—and afterwards washed.

Another plan is to fix the blood-film with alcohol and then to stain by running on a few drops of saturated watery solution of methylene blue, washing off the superfluous stain after half a minute and decolourising with weak acetic acid if necessary; the wet slide is then examined with the microscope. Or, without previous fixing with alcohol, the slide, after it has dried, may be dipped for a few seconds in water so as to wash out the hæmoglobin, dried, and then, with or without fixing, stained with methylene blue or logwood.

An inch objective and a mechanical stage with a parallel movement will enable the investigator to pass rapidly in review the whole of the blood on the slide. If filariæ are present, they will be detected readily; the unfixed hæmoglobin of the blood corpuscles being dissolved out by the watery stain, the white blood corpuscles and any filariæ that may be

present are the only coloured objects visible on the slide, and therefore at once catch the eye.

In any district in which the filaria is moderately common, out of 100 slides prepared in this way from as many individuals, probably eight or ten will be found to contain the parasite. When filariæ have been detected, the individuals from whom the parasite-bearing slides came may be used afterwards as a source of supply for further examinations and study.

Demonstration of living filariæ. — When it is desired to study the living filaria, all that is necessary is to make three or four ordinary wet preparations of the blood of a filaria-infected individual—making them during the evening or night, and ringing the cover-glasses with vaseline so as to prevent the slides from becoming dry. In such preparations the filariæ keep alive for a week, or even longer, and can readily be detected by their movements, an inch objective being used in the first instance as a searcher.

Permanent preparations.—Permanent preparations may be made by fixing very thin films of blood with alcohol or heat, staining with methylene blue, eosine, etc., and mounting in zylol balsam. It is generally advisable before fixing to wash out the hæmoglobin with water or very weak acetic acid. Logwood is perhaps the best stain; it brings out the sheath very distinctly, and picks out the nuclei. Double staining with eosine and logwood shows very well the structure of the musculo-cutaneous layer of the worm, in addition to other anatomical details.

Description of embryonic form.—Examined in fresh blood, *filaria nocturna* (Fig. 36, *a*) is seen to be a minute, transparent, colourless, snake-like organism which, without materially changing its position on the slide, wriggles about in a state of great activity, constantly agitating and displacing the corpuscles in its neighbourhood. At first the movements are so active that the anatomical features of the filaria cannot be made out. In the course of a few hours, however, the movement slows down, and then one can see that

the little worm is shaped like a snake or an eel—that is to say, that it is a long, slender, cylindrical organism, having one extremity abruptly rounded off, the other for about one-fifth of the entire length

Fig. 30. (*a*) F. larla nocturna × 300; (*b*) f. d. arna, Africa × 300; (*c*) f. Demarquai, St. Vincent × 300; (*d*) f. Ozzard, British Guiana × 300; (*e*) f. perstans, Africa × 300.

gradually tapering to a fine point. On measurement, it is found to be about $\frac{1}{85}$ of an inch in length by $\frac{1}{3000}$ to $\frac{1}{3500}$ of an inch in diameter—about the diameter of a red blood corpuscle.

When examined with a low power, it appears to be structureless; with a high power, however, a certain amount of structure can, on close scrutiny,

be made out. In the first place, it can be seen that the entire animal is enclosed in an exceedingly delicate, limp, structureless sack, in which it moves backwards

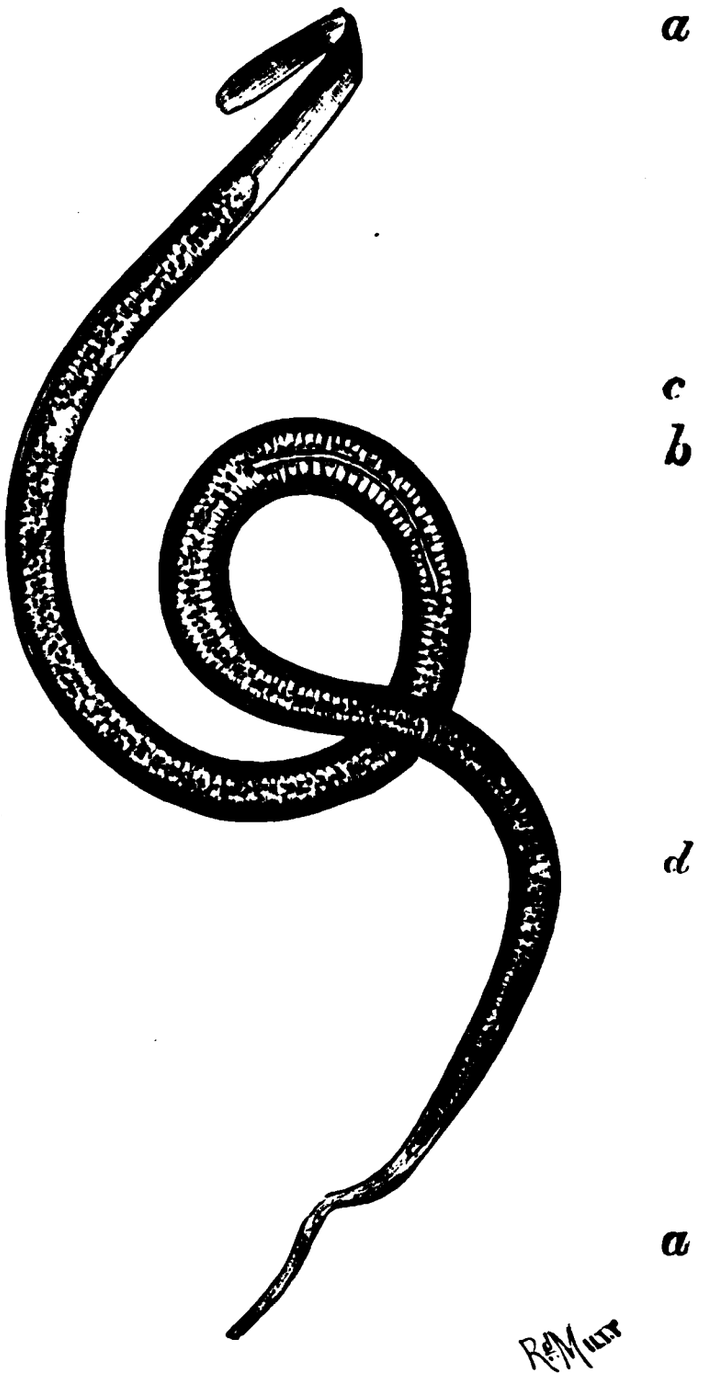

Fig. 37.—Anatomy of filaria nocturna.
a a, Sheath; *b*, central viscus; *c*, V spot; *d*, tail spot.

and forwards (Fig. 37, *a*). This sack, or "sheath," as it is generally called, although closely applied to the body, is considerably longer than the worm it encloses; so that that part of the sack which for the time being is not occupied, is collapsed and trails after the head,

or tail, or both, as the case may be. It can be seen also that about the posterior part of the middle third of the parasite, there is what appears to be an irregular aggregation of granular material which, by suitable staining, can be shown to be a viscus of some sort (*b*). This organ runs for some distance along the axis of the worm. Further, if a high power be used, a closely set, very delicate transverse striation can be detected in the musculo-cutaneous layer throughout the entire length of the animal. Besides this, if carefully looked for at a point about one-fifth of the entire length of the organism backwards from the head end, a shining, triangular V-shaped patch (*c*) is always visible. This V spot becomes still more apparent on light staining with very weak logwood. The dye brings out yet another spot (*d*), similar to the preceding, though very much smaller; this second spot is situated a short distance from the end of the tail. The former I have designated the "V spot," the latter the "tail spot." These spots are probably connected with development, the V spot being the rudiment of the future water-vascular system, or perhaps of the generative organs; the tail spot of the anus, or cloaca, and posterior part of the alimentary canal. The spots are not stained by strong logwood (*c*, *d*) or by the aniline dyes. Staining with logwood also shows that the body of the little animal is principally composed of a column of closely packed cells enclosed in the transversely striated musculo-cutaneous cylinder; at all events, many exceedingly minute nuclei are thereby rendered visible.

When the movements of the living filaria have almost ceased, by careful focussing it can be seen that the head end is constantly being covered and uncovered by a six-lipped—or hooked—and very delicate prepuce; and, moreover, one can sometimes see a short fang of extreme tenuity suddenly shot out from the uncovered extreme cephalic end, and as suddenly retracted (Fig. 37, *c*, *d*).

Filarial periodicity.—A singular feature in

the life of the embryo filaria is what is known as "filarial periodicity."

If under ordinary conditions of health and habit the blood be examined during the day, the parasite is rarely seen, or, if it be seen, only one or two specimens at most are encountered in a slide. It will be found, however, that as evening approaches, commencing about 5 or 6 o'clock, the filariæ begin to enter the

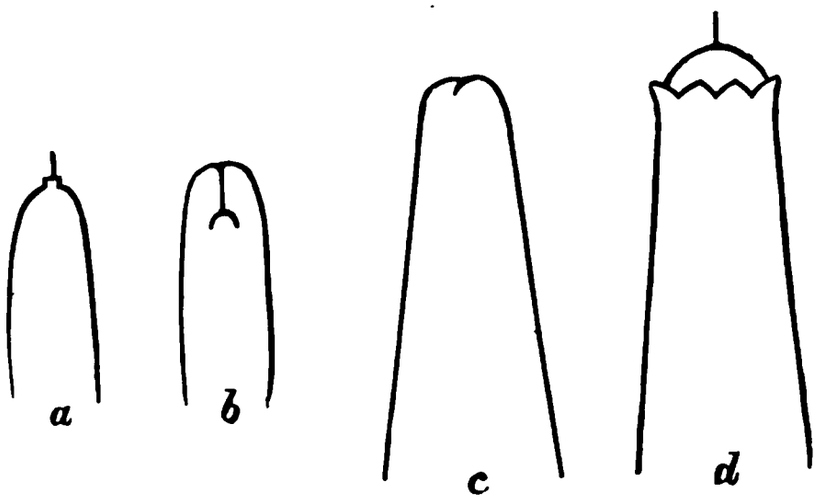

Fig. 38.—Structure of head end of filaria perstans (*a*, *b*) and of f. nocturna (*c*, *d*).

general circulation in gradually increasing numbers. The swarm goes on increasing until about midnight, at which time it is no unusual thing to find as many as three hundred, or even six hundred, in every drop of blood; so that, assuming that the parasites are evenly distributed throughout the circulation, it may be inferred that as many as forty or fifty millions are simultaneously circulating in the blood-vessels. After midnight the numbers begin gradually to decrease; by 8 or 9 o'clock in the morning the filariæ have disappeared from the peripheral blood for the day. This diurnal periodicity is, under normal conditions, maintained with the utmost regularity for years. Should, however, as Mackenzie has shown, a filarial subject be made to sleep during the day and remain awake at night, the periodicity is reversed; that is to say, the parasites come into the blood during the day and disappear from it during

the night. It cannot be the sleeping state, as some have conjectured, that brings about this periodicity, for the ingress of the filariæ into the peripheral blood commences three or four hours before the usual time for sleep, and the egress several hours before sleep is concluded, and the latter is not complete until several hours after the usual time of rising. No reasonable explanation of the cause of filarial periodicity has been given yet. A recent opportunity has enabled me to ascertain that, during their diurnal temporary absence from the cutaneous circulation, the filariæ retire principally to the larger arteries and to the lungs, where, during the day, they may be found in enormous numbers.

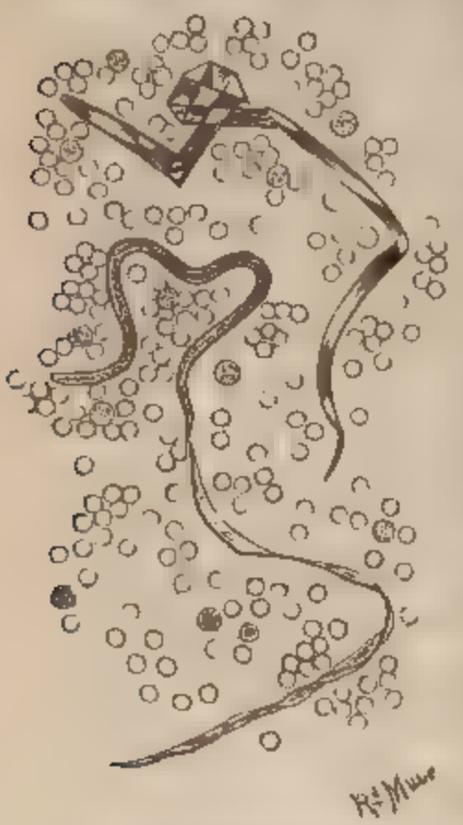

Fig. 39. Filarial ecdysis.

The mosquito the intermediate host of filaria nocturna.

Should a certain species of mosquito which has fed on the blood of a filaria-infested individual be examined immediately after feeding, the blood contained in the stomach of the insect will be found to contain large numbers of living filariæ. If a second mosquito be examined three or four hours after it has similarly fed, it will be found that the blood corpuscles in its distended abdomen have, in great measure, parted with their hæmoglobin, and that the blood plasma has in consequence become thickened, though not coagulated. If attention be directed to the filariæ

in the thickened blood, it will be seen that many of them are actively engaged in endeavouring to escape from their sheaths. The diffused hæmoglobin has so thickened the blood plasma that it has become viscid, and holds, as it were, the sheath. This change in the viscosity of the blood seems to prompt the filariæ to endeavour to escape from their sheaths. They become restless and excited. Alternately retiring towards the tail end and then rushing forward to the head end of the sheath, the imprisoned parasite butts violently against the latter in frantic effort to escape. After a time, the majority succeed in effecting a breach and in wriggling themselves free from the sheaths which had hitherto enclosed them (Fig. 39).* The filaria now swims free in the blood, the character of its movements once more undergoing a remarkable change. Hitherto, though active enough in wriggling about, the parasite did not change materially its position on the slide; but now, having become free, it moves about from place to place—"locomotes," in fact. If we dissect a mosquito at a somewhat later period after feeding, it will be found that the stomach of the insect, though still full of blood, contains very few filariæ, although their empty sheaths can be seen in abundance. If, however, we break up with needles the thorax of the insect and tease out the muscular tissue, we shall find what has become of the filariæ;

* This casting of its sheath by the filaria can be induced in ordinary blood slides by simply chilling them on ice, or by otherwise bringing about the diffusion of the hæmoglobin. The following method is usually successful: Ring with vaseline the cover-glasses of several ordinary wet preparations of finger blood obtained at night from a filarial patient; wrap the preparations separately in filter paper, and lay them, enclosed in a watertight tin box, on a block of ice, for six or eight hours—say overnight. Next morning examine them with the microscope. It will be found, as the chilled slides warm up, that wherever on the slides the hæmoglobin has become diffused and the blood lakey, the filariæ, as they gradually resuscitate from the chilling, begin to endeavour to break through their sheaths. By evening most of them have effected this, and their empty sheaths can be seen lying scattered about in the viscid blood. The blood must not be frozen.

we shall find that, after discarding their sheaths, they have quitted the stomach and entered the thoracic muscles of the insect, among which they can now be seen moving languidly (Fig. 40) By a course of serial dissections of filariated mosquitos we can ascertain that in the thorax of the insect the parasite enters on a metamorphosis which takes from six to seven days to complete—a metamorphosis eventuating in the formation of a mouth, of an alimentary canal, and of a

Fig. 40.—Filariæ in thoracic muscles of mosquito.

peculiar trilobed tail, as well as in an enormous increase in the size and activity of the young parasite (Fig. 41, *a*—*f*).

Infection of man.—About a week from the time of feeding, the mosquito, in the ordinary course of nature, lays her eggs on the surface of stagnant water, and thereafter dies, falling into the water. It is conjectured that the filaria, now a formidable-looking and very active animal about one-sixteenth of an inch in length (*f*), escapes from the dead body of the insect, and that thus, in drinking water, it obtains a chance of gaining access to the stomach of a human host. It is believed that it then bores its way through the wall of the stomach, through the intervening tissues, and finally

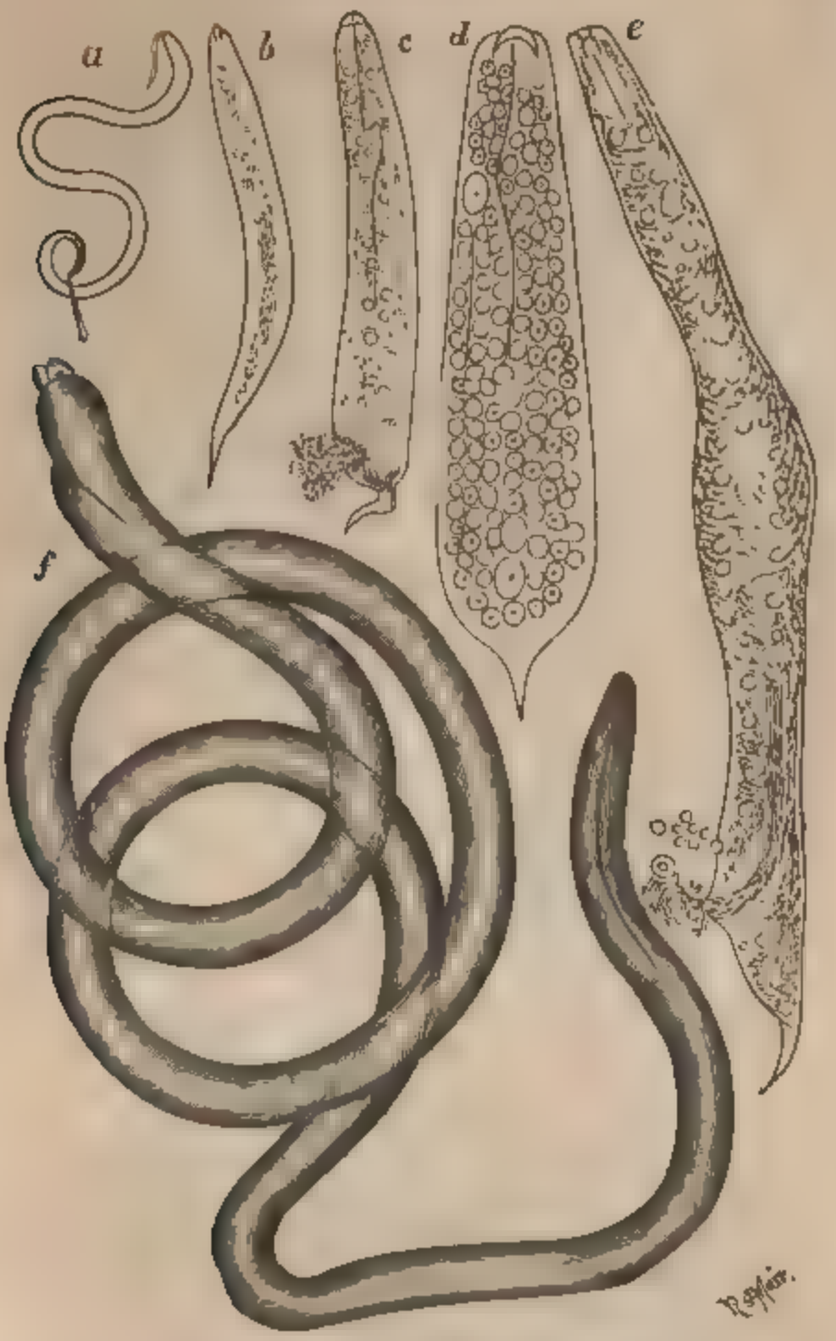

Fig. 41 — Metamorphosis of filaria in mosquito.

enters the lymphatic trunks. Arrived in one of these, it attains sexual maturity, fecundation is effected, and in due course new generations of embryo filariæ are

poured into the lymph. These passing through the glands—if such should intervene, by way of the thoracic duct and left subclavian vein, or by the lymphatics of the upper part of the body, appear in the circulation.

Such is the life-history of *filaria nocturna;* man is its definitive host, the mosquito its intermediate host. It is manifest that filarial periodicity is an adaptation of the habits of the parasite to those of the mosquito. It is also manifest that the purpose of the "sheath" with which it is provided while circulating in the human host, is to muzzle the embryo filaria and prevent its breaking through the blood-vessels, and so missing its chance of gaining access to the mosquito. The cephalic armature is adapted for piercing the walls of the mosquito's stomach, and for enabling it to travel through the tissues of the insect. In hardened sections of filariated mosquitos the parasites can be seen lying between the muscular fibres of the thorax, like so many travelling trichinæ (Fig. 40).

Parental forms (*filaria Bancrofti*). The parent filariæ have been found many times. They are long, hair-like, transparent nematodes, three or four inches

Fig. 42.—Parental form of filaria Bancrofti: female. (Natural size.)

in length (Fig. 42). The sexes live together, often inextricably coiled about each other. Sometimes they are enclosed, coiled up several in a bunch, and tightly packed in little cyst-like dilatations of the distal lymphatics (Maitland); sometimes they lie more loosely in lymphatic varices; sometimes they inhabit the larger lymphatic trunks between the glands, the the glands themselves, and, probably not infrequently, thoracic duct itself

The *female filaria* is the larger, both as regards length and thickness. The two uterine tubes, occupying the greater extent of her body, are filled with ova at various stages of development. In both sexes the oral end (Fig. 43 *b*) is slightly tapered, club-

shaped, and simple; the tail (Fig. 43 *a*, *c*) also is tapered to comparatively small dimensions, its tip being

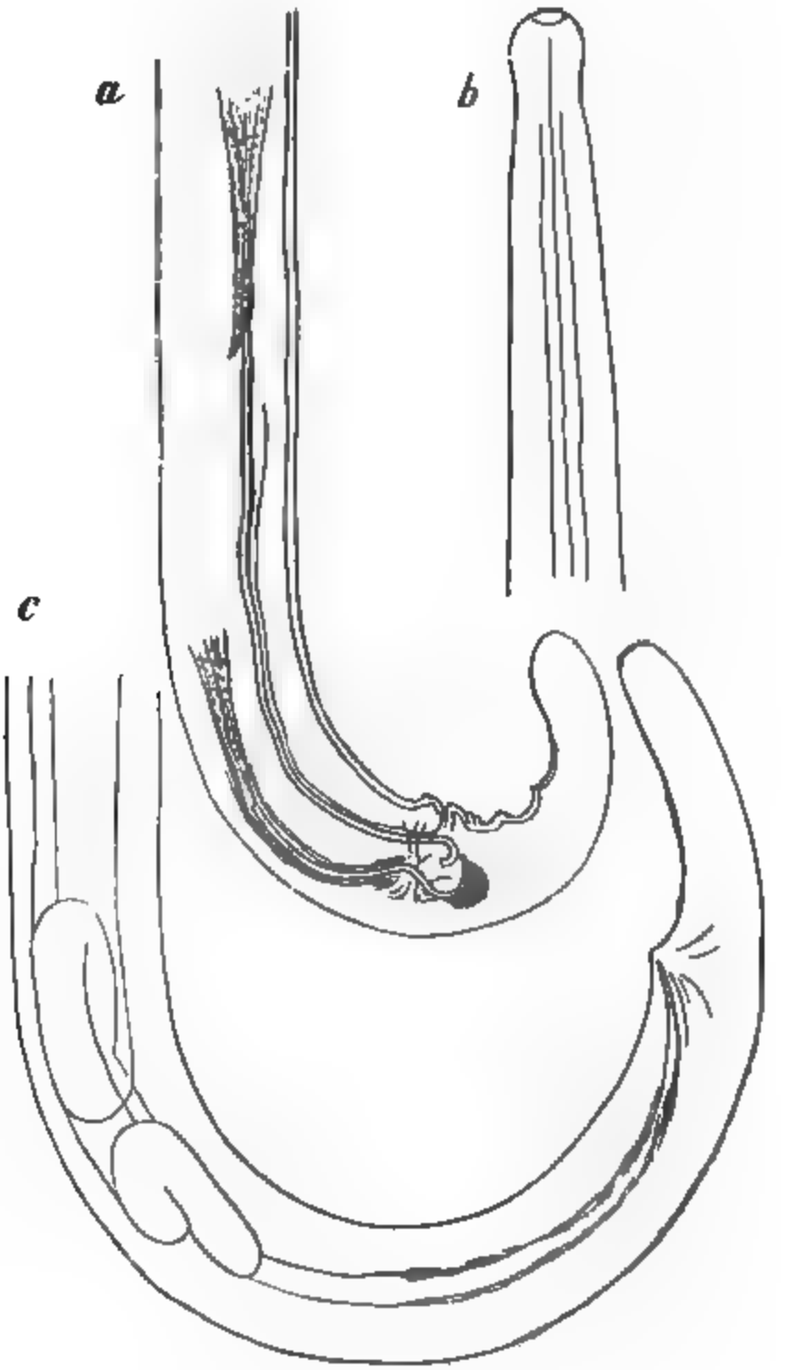

Fig. 43.—Parental forms of filaria Bancrofti.
a Tail of male; *b*, head and neck; *c*, tail of female.

rounded off abruptly. The vagina opens not very far from the mouth, the anus just in advance of the tip of the tail. The cuticle is smooth and without markings.

To the naked eye the *male worm* is characterised by its slender dimensions, by its marked disposition to curl, and by the peculiar vine-tendril-like tail, the extreme end of which straight during life (Maitland) becomes sharply incurvated after death (Fig. 43, *a*). The cloaca gives exit to two slender, unequal spicules. The existence of caudal papillæ in the male worm has not as yet been satisfactorily ascertained; analogy leads us to believe that such exist, but if they are present they must be exceedingly minute. The diameter of the female worm at her greatest breadth amounts to 0·185 mm. and the male to 0·1 mm.

These parental forms were named by Cobbold *filaria Bancrofti*, after the late Dr. Bancroft, of Brisbane, who was the first to find them.

Morbid anatomy and pathology. — *The filaria not generally pathogenetic.*—In most cases of filarial infection the parasite exercises no manifest injurious influence whatever. In a certain proportion of instances, however, there can be no doubt that it does have a very prejudicial effect on its host; and this mainly by obstructing lymphatics. The healthy, fully-formed embryo filariæ—that is to say, the filariæ which, by means of the microscope, we see in the blood—have, so far as we can tell, no pathological properties whatever; the parent worm and the immature products of conception, alone, are dangerous.

Filarial disease originates in injury of lymphatic trunks.—Roughly speaking, the filaria causes two types of disease; one characterised by varicosity of lymphatics, the other by more or less solid œdema. The exact way in which the parasite operates has not been definitely and absolutely ascertained for all types of filarial disease. Apparently, in some instances, a single worm, or a bunch of worms, may plug the thoracic duct and act as an embolus or originate a thrombus;

or the worm may give rise to inflammatory thickening of the walls of this vessel, and so lead to obstruction from the consequent stenosis or thrombosis. In other instances the minor lymphatic trunks may be similarly occluded. As an effect of either form of occlusion, the lymphatic areas drained by the implicated vessels are cut off from the general circulation; there is then a rise of lymph pressure in the occluded vessels with consequent varicosity, or there may be lymphatic œdema, or a combination of these.

Pathology of lymphatic varix.—In consequence of the rich anastomosis existing between the contiguous lymphatic areas, on filarial obstruction occurring in one of them, a compensatory lymphatic circulation is sooner or later established. But before this can be properly effected a rise of lymph pressure and a dilatation of the lymphatics in the implicated area must take place. This leads to lymphatic varix of different kinds, degrees, and situations. When the seat of filarial obstruction is the thoracic duct, the chyle poured into that vessel can reach the circulation only by a retrograde movement; consequently, this fluid may be forced to traverse in a retrograde way the abdominal and pelvic lymphatics, the lymphatics of the groin, scrotum, and abdominal wall, which, together with the thoracic duct up to the seat of obstruction, become enormously dilated. In dissections of such cases (Fig. 44) the thoracic duct has been found distended to the size of a finger, the abdominal and pelvic lymphatics forming an enormous varix a foot in diameter and many inches in thickness, concealing kidneys, bladder, and spermatic cords. In such cases, when one of the vessels of this varix is pricked or ruptures, the contents which escape are found to be white or pinkish, not limpid like ordinary lymph; they are chyle —chyle on its way to enter the circulation by a retrograde compensatory track. When the varix involves the integuments of the scrotum, the result is "lymph scrotum"; when most prominent in the groin, then

a condition of glands is produced which I have called "varicose groin glands"; when the lymphatics of the bladder or kidneys are affected and rupture from over-

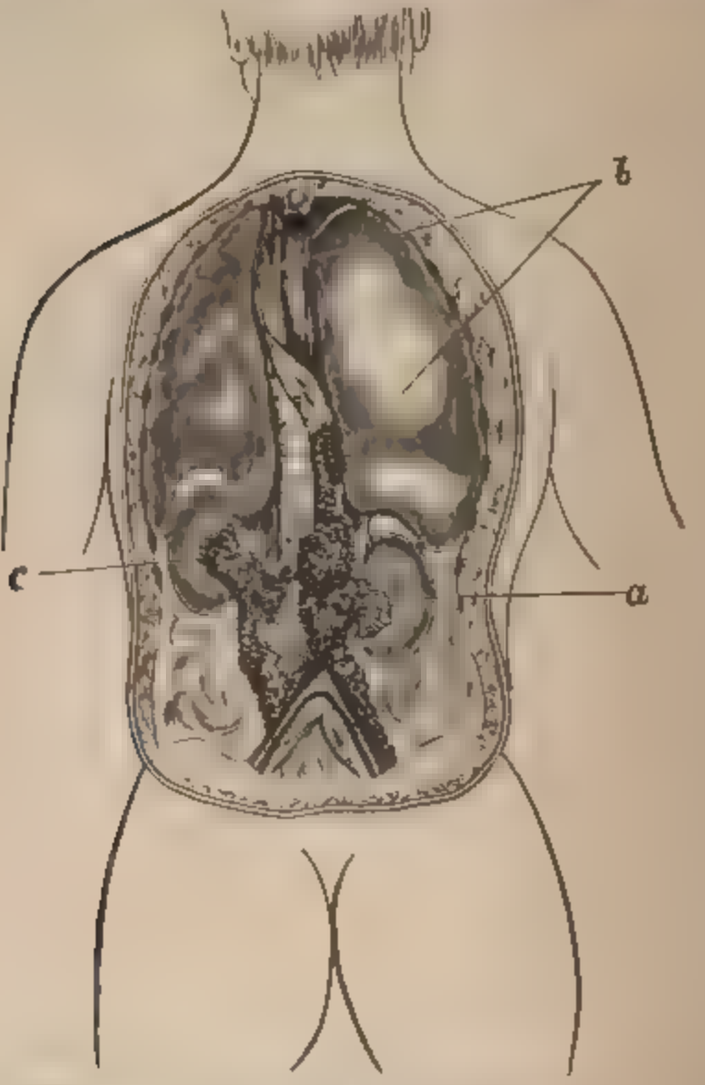

Fig. 44.—Dissection of the lymphatics in a case of chyluria. (*Mackenzie, Trans. Path. Soc., Lond.*)

a Dilated right renal lymphatics, b, thoracic duct, c, dilated left renal lymphatics.

distension, then chyluria is the result, when those of the tunica vaginalis rupture, then there is chylous dropsy of that sac—"chylocele", the same may happen in the peritoneum—chylous ascites. Occasionally varicose lymphatic glands resembling those

frequently encountered in the groins are found in the axilla; occasionally limited portions of the lymphatic trunks of the limbs are similarly and temporarily or more permanently distended. This, doubtless, is the pathology of all those forms of filarial disease characterised by visible varicosity of lymphatics, with or without lymphorrhagia.

Filariæ may disappear from the blood in such cases.—In filarial disease associated with lymphatic varix embryo filariæ are generally present in the blood as well as in the contents of the dilated vessels. Sometimes, it is true, the embryo is not found; it is highly probable, however, that these are cases of long standing, and that, had it been looked for at the commencement of the disease, the embryo would have been discovered. I have watched cases in which the embryo has disappeared in this way; though at first found in abundance in the blood, after a year or longer it ceased to appear there. The reason for this disappearance is doubtless the death of the parent parasites, an occurrence often associated with an attack of lymphangitis. It must be borne in mind, however, that although the original cause of the varix may disappear, the effects of its operation are permanent.

Pathology of elephantiasis Arabum.—*Embryos not usually present in the blood in elephantiasis.*—In those cases of filaria disease in which elephantiasis Arabum is the leading feature it is not usual, at any stage of the established disease, to find filariæ in the blood or elsewhere, unless it be in countries in which filariasis is extremely common and reinfection or extensive infection highly probable.

Reasons for regarding elephantiasis as a filarial disease.—From this circumstance—the absence of filaria embryos from the blood in elephantiasis—the question naturally arises, Why attribute this disease to the filaria? The answer to this is: (1) The geographical distributions of filaria nocturna and of elephantiasis Arabum correspond; and where elephantiasis abounds

there the filaria abounds, and *vice versâ*. (2) Filarial lymphatic varix and elephantiasis occur in the same districts, and frequently concur in the same individual. (3) Lymph scrotum, an unquestionably filarial disease, often terminates in elephantiasis of the scrotum. (4) Elephantiasis of the leg sometimes supervenes on the surgical removal of a lymph scrotum. (5) Elephantiasis and lymphatic varix are essentially diseases of the lymphatics. (6) Filarial lymphatic varix and true elephantiasis are both accompanied by the same type of recurring lymphangitis. (7) As filarial lymphatic varix is practically proved to be caused by the filaria, the inference that true elephantiasis—the disease with which the former is so often associated and has so many affinities—is attributable to the same cause, appears to be warranted.

Explanation of the absence of filariæ in the blood in elephantiasis.—If the filaria be the cause of tropical elephantiasis, how account for the absence of filaria embryos in the blood, as is the case in the vast majority of instances of this disease? The answer to this is:—Either the disease-producing filariæ have died; or the lymphatics draining the affected area are so effectually obstructed by the filaria, its products, or its effects, that any embryo filariæ they may contain, or may have contained, cannot pass along these vessels to the circulation.

We have already seen that in filarial lymphatic varix the parasite which produced the disease may die, particularly during attacks of lymphangitis; the same may occur in elephantiasis, and I believe that this does happen. I do not think, however, that this is the entire explanation.

Lymph stasis produced by filaria ova.—I have twice in filariasis found ova of the filaria in lymph; once in the lymph from a lymph scrotum, once in lymph procured by aspirating a varicose groin gland. Therefore, at times, the filaria may produce ova instead of swimming embryos. The ova of the filaria are not like the long, supple, slim, active, swimming embryo;

they are passive, more or less rigid, oval bodies nearly five times the diameter of the embryo coiled up in their interior. In consequence of their size and passive character the ova, unlike the normal free swimming embryos, are quite incapable of traversing such lymphatic glands as, in the event of their escape from the parental worm, they may be passively carried to by the lymph stream. It is an accepted fact in pathology that an essential element in the causation of elephantiasis is lymph stasis. I have ventured to conjecture that the stasis of lymph which eventuates in tropical elephantiasis is produced by embolism of the lymphatic glands by ova of the filaria. But, it may be asked, why should ova enter the lymph stream? In normal conditions the embryo filaria at birth is already fully outstretched. If ova are expelled by the parent filaria, it must be as a result of some hurrying of the process of filarial parturition. That this does occur sometimes the discovery, already mentioned, of filaria ova in the lymph fully proves; and I believe that this is really what does occur, and that it is the initial step in the development of filarial elephantiasis. We can readily understand how, in consequence of mechanical injury, to which from her exposed position she must be frequently subjected, or of some other cause, the parent filaria may miscarry. Should this happen, then the contents of her uterus will be expelled prematurely and before the ova normally lying at the upper part of her uterus have become the long, outstretched, active embryos we see in the blood. If a crowd of these passive, massive ova are carried by the lymph stream to the lymphatic glands of a limb, in the lymphatic trunks of which a female filaria is lying aborting, embolism of the afferent lymphatics of the glands must result and stasis of lymph in the limb ensue.

Inflammation necessary for the production of elephantiasis.—Lymph stasis alone does not produce elephantiasis; this has been proved by experimental ligature of lymphatic trunks. But if inflammation

occurs in an area of lymphatic congestion so produced, as it is very apt to do on the slightest injury, then elephantiasis will supervene; for, unless the lymphatics of an inflamed area are patent, the products of inflammation are not completely absorbed. Erysipelatoid inflammation, frequently recurring, is a well-recognised feature in every case of elephantiasis Arabum.

Sequence of events in elephantiasis.—The sequence of events in the production of elephantiasis is, I believe, as follows:—Parent female filaria in the lymphatic system of the affected part; injury of the filaria; premature expulsions of ova in consequence of injury; embolism of lymphatic glands by ova; stasis of lymph; lymphangitis from subsequent traumatism or other cause in the congested area, imperfect absorption of the products of inflammation; recurring attacks of inflammation, leading to gradual, intermittingly progressive, inflammatory hypertrophy of the part.

In this way I explain the production of elephantiasis by the filaria. And in this way I explain the absence from the blood of the embryos of the parasite which started the disease; they cannot pass the occluded glands. Very likely the parent worm dies at an early stage of the disease; killed by the cause which led to premature parturition, or by the subsequent lymphangitis.

The subjects of elephantiasis less liable than others to filariæ in the blood. Some years ago I made a curious observation which supports the view just stated. I received from Surgeon-Major Elcum eighty-eight slides of night blood from eighty-eight natives of Cochin. Of these eighty-eight individuals fourteen were affected with elephantiasis, seventy-four were not so affected. Of the slides coming from the seventy-four non-elephantiasis cases twenty contained filariæ, about one in every three and a half; of the fourteen elephantiasis cases only one had filariæ. Why should the elephantiasis cases have proportionately fewer

filariæ than the non-elephantiasis cases? Because in the former the existence of elephantiasis implied that a large area of their lymphatic systems was blocked, and that the blood could be stocked with embryo filariæ carried by the lymph from only a relatively small lymphatic area; there was, therefore, a proportionately small likelihood of the presence of parent filariæ having for their young an unobstructed passage to the blood.

FILARIAL DISEASES.

Enumeration of the filarial diseases.—The diseases known to be produced by *filaria nocturna* are abscess; lymphangitis; varicose groin glands; varicose axillary glands; lymph scrotum; cutaneous and deep lymphatic varix; orchitis; chyluria; elephantiasis of the leg, scrotum, vulva, arm, mamma, and elsewhere; chylous dropsy of the tunica vaginalis; chylous ascites; chylous diarrhœa, and probably other forms of disease depending on obstruction or varicosity of the lymphatics, or on death of the parent filaria.

Abscess.—Occasionally, as already mentioned, whether in consequence of blows or other injuries, of lymphangitis, or of unknown causes, the parent filaria dies. Generally the dead body is absorbed, just as a piece of aseptic catgut would be; but, sometimes the dead worm acts as an irritant and causes abscess, in the contents of which fragments of the dead filaria may sometimes be found. Such abscesses, occurring in the limbs or scrotum, will discharge in due course, or may be opened; they lead to no further trouble. Should they form, however, in the thorax or abdomen, serious consequences and even death may ensue.

Probably, in certain instances, abscess forms at times independently of the death of the parasite—in varicose glands, in lymph scrotum, in elephantiasis, or in similar areas of weakened tissues and lymphatic congestion.

The death of the parental filariæ is apt to be lost sight of as a possible cause for abscess in the subjects

of filarial infection. Deep-seated pain in thorax or abdomen, with inflammatory fever followed by hectic, and a diminution in the number of embryo filariæ in, or their entire disappearance from, the peripheral blood should, in such circumstances, suggest a diagnosis of filarial abscess and indicate exploration and, if feasible, active surgical interference.

Lymphangitis and elephantoid fever.—*Symptoms.*—Lymphangitis is a common occurrence in all forms of filarial disease, particularly in elephantiasis, varicose glands, and lymph scrotum. When occurring in the limbs, the characteristic painful, cord-like swelling of the lymphatic trunks and associated glands, and the red congested streak in the superjacent skin, are usually apparent at the commencement of the attack. Very soon, however, the connective tissue and skin of the implicated area become inflamed and tense, and high fever, preceded by severe and prolonged rigor, sets in. The attack may continue for several days, and is accompanied by severe headache, anorexia, often vomiting, and sometimes delirium. After a time the tension of the inflamed integuments may relieve itself by a lymphous discharge from the surface. Usually the attack ends in profuse general diaphoresis. The swelling then subsides gradually though not entirely, the parts remaining permanently somewhat thickened. Lymphangitis may be confined to groin glands, testis, spermatic cord, or the abdominal lymphatics.

Diagnosis.—This fever, named very appropriately by Fayrer "elephantoid fever," occurs habitually, at varying intervals of weeks, months, or years, in nearly all forms of elephantoid disease. Its tendency to recur, the severe rigor ushering it in, and the terminal diaphoresis cause it often to be mistaken for ague. The implication of the lymphatics, the local pain, the erysipelatoid swelling, the prolonged pyrexial stage, the absence of the plasmodium malariæ from the blood, the presence there very possibly of the filaria, and the powerlessness of

quinine to control the fever suffice for diagnosis. Nevertheless, error in diagnosis is very common, more particularly when the attacks recur frequently, as is commonly the case.

Treatment. The treatment should consist in removing any cause of irritation, and in rest, elevation of the affected part, cooling lotions or warm fomentations, mild aperients, opium to relieve pain, and, if tension is great, pricking or scarifying the swollen area under suitable aseptic condition.

Varicose groin glands (Fig. 45) *-Associated conditions* — Varicose groin glands are frequently

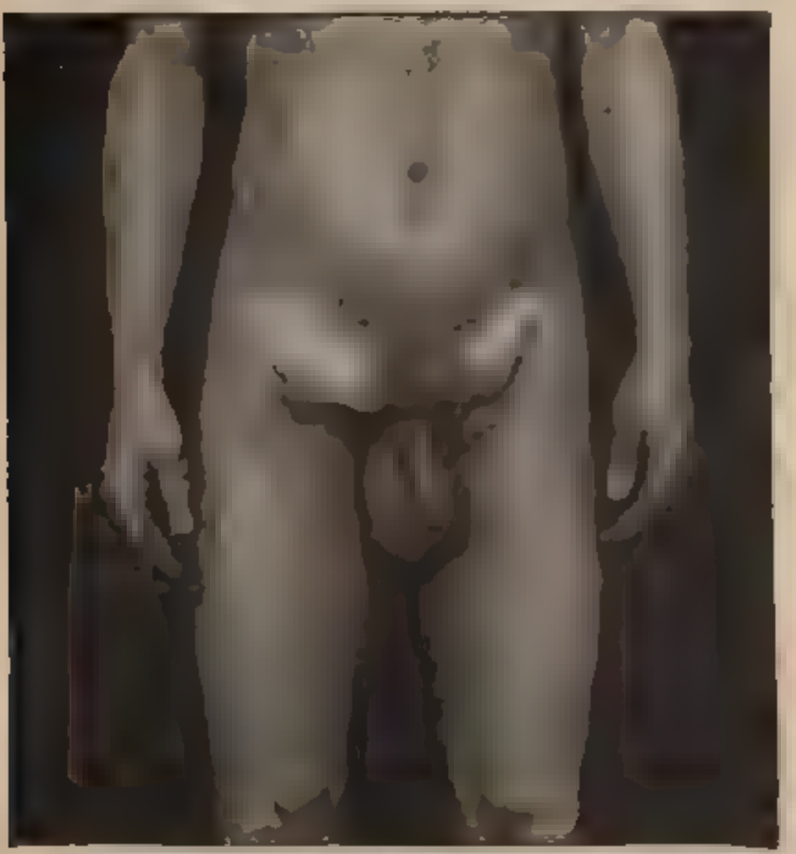

Fig. 45. -Varicose groin glands and hydrocele. (*From a patient under the care of Mr. Johnson Smith.*)

associated with lymph scrotum, sometimes with chylous dropsy of the tunica vaginalis, sometimes

with chyluria; occasionally all four conditions co-exist in the same individual.

Symptoms.—As a rule, commencing painlessly, the patient is not aware of the existence of these varicose glands until they have attained considerable dimensions. Then, a sense of tension, or an attack of lymphangitis, calls attention to the state of the groins, when certain soft swellings are discovered. These swellings may be of insignificant dimensions, or they may attain the size of a fist. They may involve both groins, or only one groin; they may affect the inguinal glands alone, or the femoral glands alone, or, and generally, both sets together.

To the touch they feel soft, doughy, and obscurely lobulated. The skin, natural in appearance, can be glided over the surface, but the tumours themselves are not movable over the subjacent fascia. Occasionally hard, kernel-like pieces can be felt in their interior, or the entire mass may be more or less indurated. On thrusting a hypodermic needle into the swellings, white or reddish chylous, or lymphous fluid can be aspirated in abundance. This fluid coagulates rapidly and usually contains living filaria embryos.

Diagnosis.—It is important to be able to diagnose these tumours from hernia, for which they are often mistaken. This can be done by observing that they are not tympanitic on percussion; that though pressure causes them to diminish they do so slowly—there is no sudden dispersion accompanied by gurgling as in hernia, on taxis being employed; that they convey a relatively slight, or no impulse on coughing; that they slowly subside on the patient lying down, and slowly return, even if pressure be applied over the saphenous or inguinal openings, on the erect posture being resumed. The cautious use of the hypodermic needle will confirm diagnosis; which would be further strengthened by the co-existence of lymph scrotum, chyluria, or chylous hydrocele, and the presence of filariæ in the blood. Chronic swellings about the groin,

cords, testes, and scrotum in patients from the tropics should always be regarded as being possibly filarial.

Pathological anatomy. — On dissection these tumours are found to consist of bunches of varicose lymphatics, and to form part of a vast lymphatic varix involving the pelvic and abdominal lymphatics.

Treatment.—Unless they give rise to an incapacitating amount of discomfort, and are the seat of frequent attacks of lymphangitis, varicose groin glands are best left alone. It must always be remembered that they are part of an anastomosis necessary to life. Should they be very troublesome and incapacitate for work, they may be removed (Maitland, *Brit. Med. Jour.*, 1897). In operating, strict aseptic methods must be practised, as septic lymphangitis readily occurs, and has frequently proved fatal in such cases. Excision is not always satisfactory, as it may be followed by lymphorrhagia at the seat of the wound, by excessive dilatation of some other part of the implicated lymphatic area, by chyluria, or by elephantiasis in one or both legs.

It is said (Azema) that these glands tend to diminish in size after forty. I cannot confirm this statement from personal observation.

Similar varicose dilatation of the axillary glands is sometimes, though much more rarely, met with. Bancroft designated these varicose axillary and groin glands "helminthoma elastica."

Cutaneous and deeper lymphatic varices. —Occasionally cutaneous lymphatic varices are met with on the surface of the abdomen, on the legs, arms, and probably elsewhere. Sometimes they are permanent; sometimes, when more deeply situated, they constitute little swellings which come and go in a few hours. I believe these latter often depend on the actual presence of parent filariæ in the tumour. Such varices are evidence of lymphatic obstruction. Their contents may be milky and chylous, or straw-coloured and lymphous, according to situation and connections.

Thickened lymphatic trunks.—Surgeon-Lieut.-Col. Maitland (*loc. cit.*) has frequently seen in Madras cases of lymphangitis in which, after the initial swelling and inflammation had subsided, a line of thickening remained. On excising this thickened tissue and carefully dissecting it, he has found minute cyst-like dilatations of the lymphatic involved, and in these cysts adult filariæ coiled up, sometimes dead, sometimes alive. The lymphangitis, he believes, is caused in these cases by the death of the filariæ. Daniels has made similar observations in British Guiana. Such a case I recently saw under the care of Dr. Abercrombie at Charing Cross Hospital in London. On the subsidence of a filarial lymphangitis of the arm a thickening, about the size of a finger-tip, remained on the forearm. Believing that it contained adult filariæ, this thickening was excised by Mr. Young and placed in normal salt solution. Eight hours later the mass was carefully dissected, and a living female filaria, about four inches in length, was turned out. The parasite continued to live and swim about actively in the salt solution for nearly two hours (*Brit. Med. Jour.*, April 24, 1897).

Lymph scrotum (Fig. 46).—*Symptoms.*—In this disease the scrotum is more or less enlarged. Though usually silky to the touch, on inspection the skin presents a few, or a large number of, smaller or larger lymphatic varices which, when pricked or when they open spontaneously, discharge large quantities of milky, or sanguineous-looking, or straw-coloured, rapidly-coagulating lymph or chyle. In some cases eight or ten ounces of this substance will escape from a puncture in the course of an hour or two; it may go on running for many hours on end, soiling the clothes of the patient and exhausting him. Usually embryo filariæ can be discovered in the lymph so obtained, as well as in the blood of the patient. In a large proportion of cases of lymph scrotum the inguinal and femoral glands, either on one or on both sides, are varicose.

Probably provoked by injury in rubbing against the thighs and clothes, erysipelatoid inflammation and elaphantoid fever are frequent occurrences Abscess

Fig 46. Lymph scrotum with varicose groin glands. (*From a photograph by Dr. Rennie, Foochow.*)

is not uncommon. In time, in a proportion of cases, the scrotum tends to become permanently thickened and to pass into a state of true elephantiasis.

Treatment.— Unless inflammation be a frequent occurrence, or there be frequent and debilitating lymphorrhagia, or unless the disease is tending to pass into true elephantiasis, lymph scrotum—kept

scrupulously clean, powdered, suspended, and protected —had better be left alone. Should, however, for these or other reasons, it be deemed expedient to remove the diseased tissues, this can be effected easily. The scrotum should be well dragged down by an assistant whilst the testes are pushed up out of the way of injury. A finger knife is then passed through the scrotum, and in sound tissues, just clear of the testes, and the mass excised by cutting backwards and forwards. No diseased tissues, and hardly any flap, should be left. Sufficient covering for the testes can be got by dragging on the skin of the thighs, which readily yields and affords ample covering It is a very common, but a very great mistake to remove too little. As a rule, the wound, if carefully stitched and dressed antiseptically, heals rapidly.

In consequence of this sudden and violent interference with an extensive varix, of which that in the scrotum is but a part, chyluria and sometimes elephantiasis of a leg may supervene. The patient should be warned of this possibility.

Chyluria.—*Pathology.*—When a lymphatic varix in the walls of the bladder, the consequence of filarial obstruction in the thoracic duct, ruptures, there is an escape of the contents of the varicose lymphatics into the urine. Chyluria is the result.

Symptoms —This disease frequently appears without warning; usually, however, pain in the back and aching sensations about the pelvis and groins — probably caused by great distension of the lymphatic varix—precede it. Retention of urine, from the presence of chylous coagula, is sometimes the first indication of serious trouble. Whether preceded by aching, or by retention, or by other symptoms, the patient becomes suddenly aware that he is passing milky urine. Sometimes, instead of being white, the urine is pinkish or even red, sometimes white in the morning, it is reddish in the evening, or *vice versâ*. Sometimes, whilst chylous at one part of the day, it is perfectly limpid at another. Great variety in this

respect exists in different cases, and even in the same case from time to time, depending on temporary closure of the rupture in the lymphatic, and also on the nature of the food.*

Physical characters of chylous urine.—If chylous urine be passed into a urine glass and allowed to stand, as a rule, within a very short time, the whole of the urine becomes coagulated. Gradually the coagulum contracts until, at the end of some hours, a small, more or less globular clot, usually bright red or pinkish in colour, is floating about in a milky fluid. Later, the milky fluid separates into three layers. On the top there is formed a cream-like pellicle; at the bottom a scanty reddish sediment, sometimes including minute red clots; in the centre the mass of the urine forms a thick, intermediate stratum, milky white or reddish white in colour, in which floats the contracted coagulum. If a little of the sediment be taken up with a pipette and examined with the microscope, it is found to contain cells like red blood cells, lymphocytes, granular fatty matter, epithelium and urinary salts, and, mixed with these in a large proportion of cases though not in all, filaria embryos. The middle layer contains much granular fatty matter; whilst the upper cream-like layer consists of the same fatty material in greater abundance, the granules tending to aggregate into larger oil globules. If a small portion of the coagulum be teased out, pressed between two slides, and examined with the microscope, filariæ, more or less active, may be found in the meshes of the fibrine. If ether be shaken up with the milky urine, the fat particles are dissolved out and the urine becomes clear; the fat may be recovered by decanting and evaporating the ether which floats on the urine.

* The sanguineous appearances so frequently seen in chylous urine, and in other forms of filarial lymphorrhagia, depend on the formation of blood corpuscles in lymph long retained in the varicose vessels, and is a result of the normal evolution of the formed elements in that fluid. There is no rupture of blood-vessels, as some have asserted.

Boiling the urine throws down a considerable precipitate of albumin.

Recovery and relapse.—Chyluria comes and goes in a very capricious manner. Sometimes the urine remains steadily chylous for weeks and months, and then suddenly, without obvious cause, becomes limpid and natural-looking, and free from fat or albumin. Later a relapse will occur, again to disappear after an uncertain time; and so on during a long course of years.

Retention of urine.—Retention of urine is not an unusual occurrence; it is produced by the formation of coagulum in the bladder. The retention usually gives way after a few hours of distress, worm-like clots being passed.

Constitutional effects.—Although chyluria is not directly dangerous to life, yet, being prolonged, it gives rise to pronounced anæmia, depression of spirits, feelings of weakness and debility, and tends to incapacitate the patient for active, vigorous life.

Exciting causes of chyluria.—Chyluria is very liable to occur, either for the first time, or as a relapse, in pregnancy or after childbirth; the disturbance of the pelvic lymphatics in this state, and the muscular efforts attending labour apparently causing rupture of pelvic lymphatics previously rendered varicose by filarial obstruction of the thoracic duct. In men, running, leaping, and violent efforts generally are sometimes assigned as its cause; usually, however, the exciting cause is not discoverable.

Treatment.—The treatment of chyluria should be conducted on the same lines as the treatment for inaccessible varix elsewhere; that is to say, by resting and elevating the affected part, and thereby diminishing as far as possible the hydrostatic pressure in the distended vessels. Many forms of medicinal treatment have been advocated. Because during treatment with some drug a chyluria has subsided, curative properties have been incorrectly attributed to the drug which was being taken at the time. The best results are got

by sending the patient to bed, elevating the pelvis, restricting the amount of food and fluid—especially fatty food, gentle purgation, and absolute rest. It will be found that a day or two of treatment on these lines is often followed by temporary, perhaps prolonged, cessation of the chyluria. The drugs which have been particularly lauded in the treatment of this disease are gallic acid in large doses, benzoic acid in large doses, glycerine, the tincture of the perchloride of iron, decoction of mangrove bark, chromic acid, quinine, salicylate of soda, ichthyol, and *nigella sativa*. I do not believe that these substances have any influence whatever in stopping the lymphorrhagia. Neither do I believe that thymol, recommended by Lawrie, or methylene blue, recommended by American writers, have any effect whatever, either on the filaria or on the disease it gives rise to; since their first recommendation both of these drugs have been tried, but in other hands have failed.

Filarial orchitis.—Several French writers describe under the name "malarial orchitis" a special form of inflammation of the testes, and here and there in Indian medical literature allusion is made to the same, or a similar subject. I have many times seen filarial orchitis, but I cannot say I have seen orchitis of purely and unquestionably malarial origin. The fever attending filarial orchitis—which is usually associated with lymphangitis of the spermatic cord and perhaps with inflammation of the scrotum, like ordinary elephantoid fever, resembles very closely a malarial attack, and may be mistaken for this. Without absolutely denying the existence of such a disease as malarial orchitis, I would suggest that the affection described by the French and Indian writers referred to, and endemic inflammations of testes, spermatic cords, and scrotum generally, are of filarial origin.

ELEPHANTIASIS.

Its prevalence.—Elephantiasis is by far the most frequent manifestation of filarial infection, and is

exceedingly common in some of the endemic districts. Thus in certain districts in Cochin about 5 per cent. of the population; in Samoa about every second individual; in Huahine seven-tenths of the adult male population are affected. In many other tropical and sub-tropical countries, if not so common as in those just mentioned, elephantiasis is, nevertheless, common enough.

Parts affected.—In 95 per cent. of the cases the lower extremities—either one or both—alone, or in combination with the scrotum or arms, are the seat of the disease. The foot and ankle only, or the foot and leg, or the foot, leg, and thigh, may, each or all, be involved. The scrotum is also a common situation for elephantiasis. The arms are more rarely attacked; still more rarely the mammæ, vulva, and circumscribed portions of the integuments of the limbs, trunk, or neck.

The recurring erysipelatoid attacks. The disease in any of these situations commences with a rapidly evolved lymphangitis, dermatitis, and cellulitis, accompanied by elaphantoid fever. On the subsidence of the acute symptoms the skin and subcutaneous fascia of the affected part do not quite resume their original proportions, the inflammatory effusion not being completely absorbed, some permanent thickening remains. Recurrences of this inflammation once or twice a month, or perhaps once in six months, or every twelve months, or even at longer intervals, add a little each time to the bulk of the limb or scrotum; thus, gradually, an enormous swelling may be built up. Occasionally, though very rarely, enlargement may progress after one, two or more initial inflammatory attacks and without further recurrence of these.

Clinical characters of the swelling.—The affected part is greatly increased in bulk. The surface of the skin, in confirmed elephantiasis especially, is rough and coarse; the mouths of the follicles are sometimes unusually distinct; the papillæ and glands are either hypertrophied or atrophied; the hair is coarse and

sparse; the nails rough, thick, and deformed. Around joints the thickened integuments are thrown into folds, the comparatively smooth sided and deep interlying sulci permitting limited movement. There is no distinct line of demarcation between

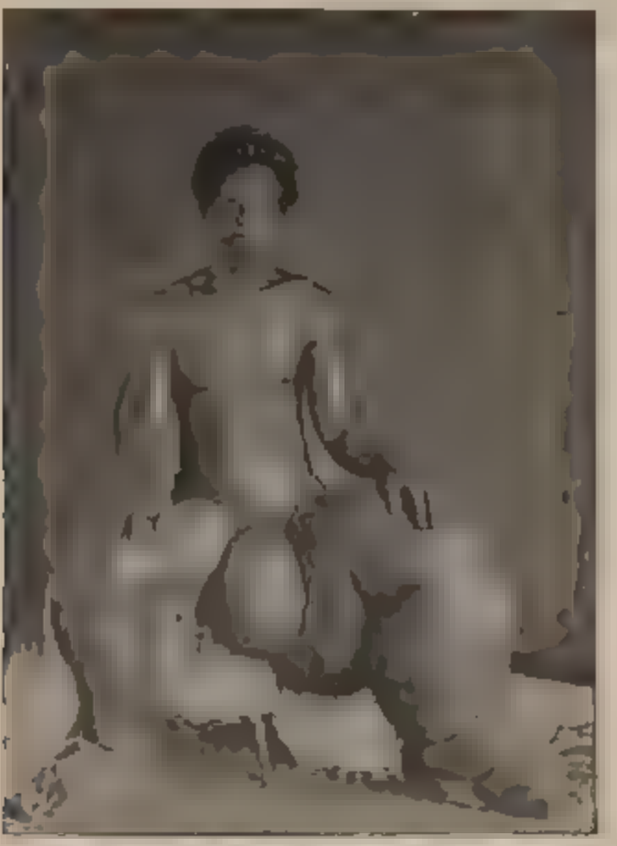

Fig. 47.—Elephantiasis of legs, scrotum, and right arm slightly affected. (*From a photograph by Dr. Turner, Samoa.*)

healthy and diseased skin. The implicated integuments are hard, dense, pit but slightly if at all on pressure, and cannot be pinched up or freely glided over the deeper parts.

Its macroscopic anatomy.—On cutting into the swelling, the derma is found to be dense, fibrous, and enormously hypertrophied. The subjacent connective tissue is increased in bulk having, especially in the case of the scrotum, a yellowish, blubbery appearance

from a sort of lymphous infiltration; a large quantity of this fluid wells out on division of the tissues. The muscles, nerves, and bones are not necessarily diseased, although in rare instances they may be degenerated and slightly or considerably atrophied from pressure. The blood vessels are large; the lymphatics dilated; the associated lymphatic glands, both of the same side and very often of the opposite side, enlarged and dense.

Elephantiasis is permanent.—Though in recent cases elephantiasis of the limbs may be much reduced by treatment, the disease is never permanently recovered from.

Elephantiasis of the legs (Fig. 47).—Elephantiasis of the lower extremities is usually, though by no means always, confined to below the knee. The swelling may attain enormous dimensions and involve the entire extremity, the leg or legs attaining a circumference, in aggravated cases, of several feet

Treatment. In the treatment of elephantiasis of the leg the patient should be encouraged to persevere with elastic bandaging, massage, and elevation of the limb. Ligature of the femoral artery has been practised it is probably useless, and is certainly not a justifiable method of treatment. Sometimes, in extreme cases, good results are got from excision of redundant masses of skin, a longitudinal strip of three or four inches in breadth by a foot or more in length being dissected off Electrolysis and mercury have also been used, I question their value. During the acute attacks, tension may be relieved by aseptic punctures with a sharp lancet. At all times the limb must be carefully guarded from injury, and shoes and trousers worn. Slight injuries provoke the inflammatory recurrences Wading in water, prolonged standing, violent exercise, and exposure to a hot sun are injurious, and should be avoided as far as possible.

Elephantiasis of the Scrotum (Fig. 48).—*Weight of tumours.*—Elephantiasis of the scrotum, or "scrotal tumour" as it is sometimes called, may attain

an enormous size. Ten, fifteen, or twenty pounds are common weights for these tumours, and forty or fifty pounds is by no means uncommon; the largest recorded weighed 224 lbs.

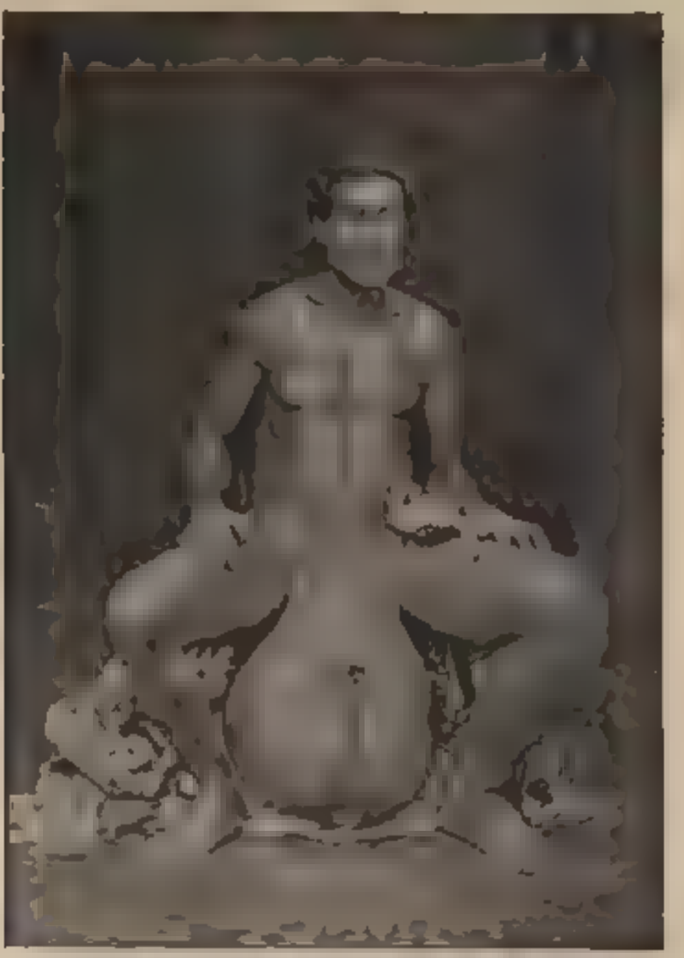

Fig. 48. Elephantiasis of the scrotum; left testicle slightly affected. (From a photograph by Dr. Turner, Sydney.)

Anatomical characters.—There are certain points in the anatomy of scrotal tumour which the operating surgeon must bear in mind. These tumours consist of two portions (Fig. 49): First, a dense rind of hypertrophied skin (A *e*), thickest towards the lower part and gradually thinning out as it merges above into the sound skin of the pubes and thighs; second, enclosed

in this rind, a mass of lax, blubbery, dropsical, easily torn through, areolar-tissue, in which testes, cords, and penis are embedded. The shape of the tumour is more or less pyriform. The upper part, or neck, on transverse section (B) is triangular, the base (B *k*) of the triangle being in front, the apex (B *j*) —usually somewhat bifid from dragging on the gluteal folds—towards the anus, the sides (B *h*) towards the thighs. In the latter situation the skin, though usually more or less diseased, is, from pressure, softer and thinner than elsewhere, tempting the surgeon to utilise it for the formation of flaps—not always a wise proceeding. The penis (A *a*, B *f*) always lies in the upper and fore part of the neck of the mass; it is firmly attached to the pubes by the suspensory ligament. The sheath of the penis is sometimes specially hypertrophied, standing out as a sort of twisted ram's horn like projection on the anterior surface of the tumour; this, however, is unusual. Generally, the sheath of the penis is incorporated in the scrotal mass, the prepuce being dragged on and inverted so as to form a long channel leading to the glans penis and opening (A *l*) half way down, or even lower, on the face of the tumour. The testes (A *c*), buried in the central blubbery tissue, usually lie towards the back of the tumour, one on either side, in large tumours generally nearer the lower than the upper part. They are more or less firmly attached to the under part of the scrotum by the hypertrophied remains of the gubernaculum testis (A *d*); a feature to be specially borne in mind by the surgeon. As a rule, both testes carry

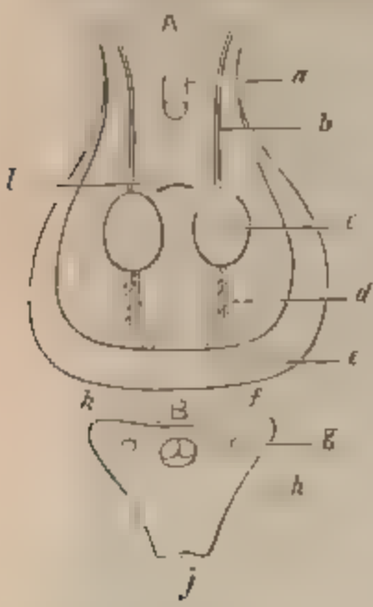

Fig. 4. Diagram of the anatomy of elephantiasis of scrotum.

large hydroceles with thickened tunicæ vaginales. The spermatic cords, also (A *b*, B *g*), are thickened and greatly elongated. The arteries supplying these enormous growths are of considerable size; the veins, too, are very large and, as they permit regurgitation of blood from the trunk, are apt to bleed freely.

Their importance.—Beyond inconvenience from their weight, the presence of the cumbersome mass between the legs, the suffering attendant on recurring attacks of inflammation and elephantoid fever, the sexual disability, and the unsightliness, these tumours are not of great importance; they do not, as a rule, directly endanger life. They may grow rapidly or slowly; they may attain a large size in two or three years, or they may be in existence for years and at the end of this time amount to little more than a slight thickening of the scrotum. Occasionally, in large tumours, portions of the mass become gangrenous, or abscess may form, and in this way life may be endangered; this is not usual, however.

Treatment.—Scrotal tumour, so soon as it becomes unsightly or inconvenient, should be removed. Often after thorough removal of all the diseased integuments, elephantoid fever, which before may have been frequent, ceases to recur.

Treatment preliminary to operation. — If the tumour is of considerable size, the patient should keep his bed for a day or two before operation, the mass being suspended so as to drain it of fluid and blood. It is thus rendered lax, and the operator is enabled to ascertain by palpation the position of the testes and, if such chance to be present, of hernia—a not very unusual complication. The possibility of undescended testes should not be overlooked.

Operation.—Before making provision for the prevention of hæmorrhage the operator should mark out by shallow cuts the line at which he proposes to separate the tumour, care being taken that these guiding incisions run through and include only absolutely sound skin; if the latter precaution be neglected,

disease is very liable to recur in the scar or flaps. First, the tumour is turned up and a shallow cut is drawn in sound skin across the perineum in front of the anus. The tumour being allowed to fall down, a similar cut is made across the pubes. The corresponding extremities of these two cuts are then united either by a straight cut, or, if there be a little sound skin on the thigh aspects of the tumour, by semilunar incisions.

Assistants then firmly draw down the scrotum as far as possible and the surgeon, if he deem it desirable,

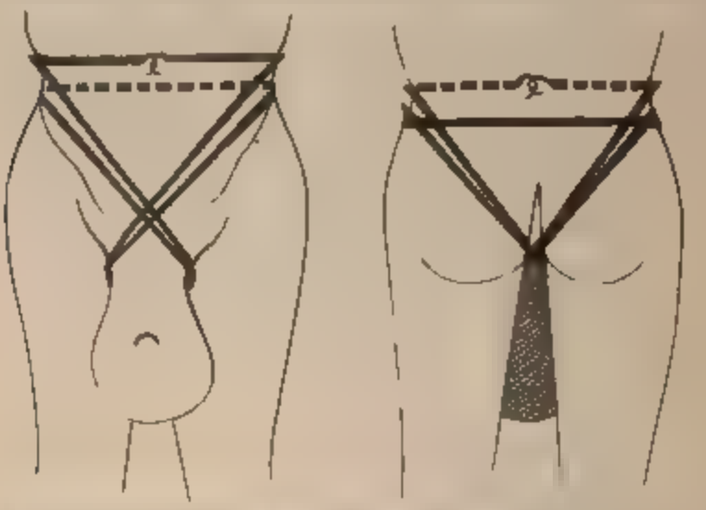

Fig. 50. Diagram showing operation for elephantiasis of scrotum; the rubber cord in position. (*M'Leod.*)

applies elastic webbing over the mass so as to expel the blood it contains. Next, a stout rubber cord is wound, figure of 8 fashion, round the neck of the tumour, well above the guiding incisions, and over the pelvis, and firmly secured (McLeod) (Fig. 50). Or the rubber cord is wound round the neck of the tumour only, being kept in place by four strips of bandage passing in front and behind under the cord, and firmly tied over another strip of bandage encircling the waist.

The testes and cord are first dissected out through long perpendicular incisions made in front, the remains of the gubernacula testes being hooked up with the finger and snipped through with scissors. The channel

of the prepuce is next slit up, the incision being carried up to the pubic limiting mark. The penis can then be shelled out, the prepuce being first cut through around the corona glandis. If lateral flaps can be formed of sound skin they are then dissected up. The perineal and pubic incisions are now deepened and, assistants holding the testes and penis well out of the way, the neck of the tumour is cut through close to the perineum and pubes. Gaping vessels are all carefully ligatured, and redundant tunica vaginalis—if hydroceles be present—excised. The rubber cord is then removed.

When hæmorrhage has been controlled, the posterior halves of the flaps are brought together by sutures, the anterior halves being united over the testes to the pubic cut. The penis will therefore emerge from the point where the horizontal line meets the perpendicular line of what is now a T- or Y-shaped wound. If no flaps have been made, the testes may be fixed by stitching any tag of tissue connected with them to the perineum, and the dimensions of the wound reduced as much as possible by stitching up the corners at the pubes and perineum.

In dressing it is of importance that the raw surfaces be covered by some aseptic *non-fibrous* protective —such as oiled silk—before the antiseptic dressing is applied. A fibrous dressing next the raw surfaces is troublesome, as it sticks to the wound and is painful and difficult to remove. The dressing should be massive, well padded, and kept in place by an eight-tailed bandage secured in front and behind to a strap round the waist, a hole being cut in front for the penis to emerge. The large wound generally does well. Skin grafting should be practised freely and early, especially round the root of the penis.

Mortality from operation.—The mortality from these formidable-looking operations, if they are carefully done, is small, and need not exceed 5 per cent. The results are very satisfactory as a rule, the functions of the organs being retained or restored.

FIG. 81.—ELEPHANTIASIS OF VULVA

(From a photograph by Dr. Walter H. B. Macdonald.)

Elephantiasis of the arms. This is comparatively rare. Allowing for the differences between the upper and lower extremities as regards gravitation of fluids, the symptoms and pathology of elephantiasis of the arm are the same as those of elephantiasis of the legs. Beyond the judicious employment of massage and elastic bandaging little can be done in the way of treatment.

Elephantiasis of the vulva and mammæ. Elephantiasis of the vulva (Fig 51) and mammæ (Fig 52) is still rarer. Where growth has become inconveniently large the diseased tissues should be removed Instances are on record in which the integuments of the mammæ have become so thickened, heavy and elongated, that the organ has descended to the pubes and even to the knee. One such tumour weighed twenty one pounds after removal. Tumours of the labia or of the clitoris, similarly, may attain a great size—eight or ten pounds, or even more.

Elephantiasis of limited skin areas. Dr. Corney, of Fiji (*Lancet*, April 6th, 1889), states that pedunculated elephantoid tumours, springing from the groin or from the anterior surface of the thigh, are not uncommon in Fiji. One such tumour which he removed weighed twenty pounds Dr Daniels (*Brit Guiana Med Ann*, 1896) has seen, both in Fiji and in Demerara, several cases of this description (Fig. 53) Dr. Silcock (*Indian Med. Gaz.*, July, 1895) describes a pedunculated tumour of this nature which he removed from the neck of an East Indian, and which weighed, after removal, thirty pounds I have often seen limited areas of elephantoid thickening of the skin, particularly on the thighs. These conditions are easily dealt with by simple operations

Chylous dropsy of the tunica vaginalis, and of the peritoneum; chylous diarrhœa. Chylous dropsy of the tunica vaginalis is not an unusual occurrence in the tropics. A fluctuating swelling of the tunica vaginalis, which does not transmit light, and which is associated possibly with

Fig. 52.—Elephantiasis of mamma (left side) and foot also affected.

(*From a photograph by Dr Davies, Samoa.*)

lymph scrotum, with varicose groin glands, with chyluria, or with filariæ in the blood, would suggest a diagnosis of this condition. These collections of chylous fluid in the tunica vaginalis generally contain

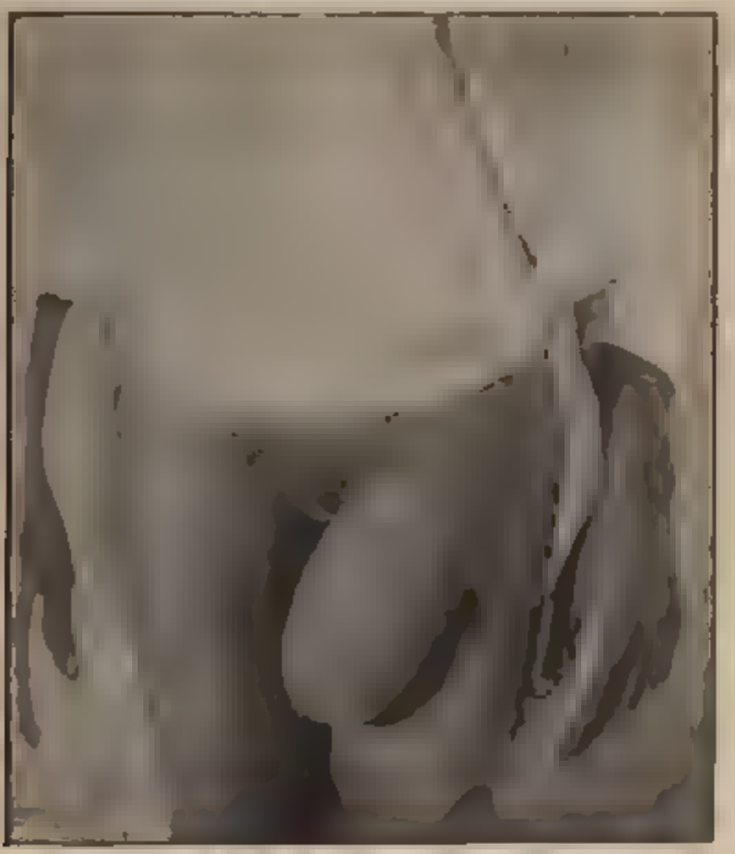

Fig. 5[illegible]-Pedunculated groin elephantiasis. (*From a photograph by Dr. Daniels, Demerara.*)

enormous numbers of filaria embryos. They may be treated as ordinary hydroceles, either by aseptic incision or by injection.

Chylous dropsy of the peritoneum, and chylous diarrhœa of filarial origin are very rare.

Prophylaxis of filarial disease; a pure water supply. The prevention of filarial disease resolves itself into securing a water supply uncontaminated by mosquitoes. With this in view, shallow and unprotected wells and tanks must not be used as sources of drinking water; tanks and buckets for

other slides as many as forty or fifty. In size and shape five out of six resemble very closely filaria perstans (p. 495)—that is to say, they are blunt-tailed, have no sheath, and are very minute (·173 to ·240 mm. by ·0043 to 005 mm., Daniels). But along with the blunt-tailed filariæ and on the same slides there occurs a sharp-tailed form, also very minute and resembling, though perhaps more slender, filaria Demarquaii. There are about five blunt-tailed parasites to every sharp-tailed parasite. Drs. Ozzard and Daniels (*Brit. Guiana Med. Ann.*, 1897) have confirmed this discovery. Both of these observers have had abundant opportunity of examining filaria Ozzardi alive, and state in letters to me that they regard the sharp- and blunt-tailed worms as phases of the same parasite. Dr. Ozzard considers that the worm when alive has the power of retracting the tip of its tail. Dr. Daniels, apparently, is of opinion that the sharp appearance of the tail in some specimens is produced in the act of dying. Filaria Ozzardi is sheathless. It is present at all times of the day and night in the peripheral blood, and possesses distinct powers of locomotion, similar to those of filaria perstans.

It is possible that the blunt-tailed and the sharp-tailed parasites belong to different species. If such be the case, then it is also possible that the sharp-tailed species is f. Demarquaii, and the blunt-tailed f. perstans, or that both, or either, may be entirely new species. Adopting the view of Ozzard and Daniels, that the blunt-tailed and the sharp-tailed are but phases of the same embryo, it follows that it must belong to an entirely new species; for, in that case, filaria Ozzardi cannot be filaria perstans, because in a large number of slides from Africa containing filaria perstans which I examined with this point in view, I did not once encounter a sharp-tailed filaria. Similarly, in a considerable number of slides from St. Vincent, West Indies, containing filaria Demarquaii, I did not encounter one blunt-tailed parasite;

filaria Ozzardi, therefore, cannot be filaria Demarquaii. Further observations are required before this point can be considered as settled. Recently, having found one case in which sharp-tailed filariæ were alone present, Daniels inclined to regard the two forms as the young of distinct species, f. perstans being one of them. I incline to this view.

I do not know as yet of any pathological condition attributable to these new and interesting blood worms.

Parental form.—In a letter Dr. Daniels tells me that he has recently found parental filariæ—male and female—at the *post-mortem* examination of two Demerara Indians whose blood, during life, contained both blunt- and sharp-tailed embryos. The mature worms, apparently numerous, were about three inches in length and very slender—about one-third the diameter of f. Bancrofti. They were, therefore, not f. Magalhãesi. The head is somewhat club-shaped and shows no papillæ. The tail of the male is much coiled and carries at least one long protruding spicule. These worms were found in the mesentery, and fat at the base of the mesentery, in one case; in the other "not only in the mesentery and abdominal fat, but also in the subpericardial fat." The embryos *in utero*, Dr. Daniels states, were all blunt-tailed. Possibly he has found the mature form of f. perstans. (*Brit. Med. Journ.*, April, 1898.)

FILARIA PERSTANS. (Fig. 36, *e*.)

Geographical range.—This parasite is very common in the blood of the natives of large districts in West Africa. I have found it in natives from Old Calabar and from the Congo—both in the coast negroes and in those from the interior. In the endemic districts it occurs in about half the population. Prof. Firket, of Liége, has confirmed this observation as regards the Congo district. Sometimes it occurs along with f. diurna and f. nocturna in the same individual. I have never found it in West Indian negroes, nor, in fact, in natives of any country except

West tropical Africa, and, possibly, in Demerara Caribs.

Its characters. — Filaria perstans observes no periodicity, being present in the blood both by day and by night. In this respect it resembles filaria Demarquaii and f. Ozzardi; and, like these, in size, shape, and anatomical detail it differs very materially from filaria nocturna and f. diurna.

It measures, on an average, $\frac{1}{125}$ inch in length by $\frac{1}{5500}$ inch in breadth; but, as it possesses to a remarkable degree the power to elongate and to shorten itself, these measurements do not always apply. On the whole, however, it is manifestly much smaller than filaria nocturna and diurna. It is further distinguished from these filariæ by the entire absence of a sheath, and by the characters of its caudal end, which is invariably truncated and abruptly rounded-off. The taper terminating in the tail extends through quite two-thirds of the entire length of the animal. Further if the head be carefully observed with a high power, a fang can generally be easily seen—much more easily than the corresponding structure in filaria nocturna —in constant play, shot out and retracted. From indications in stained specimens I judge that it possesses a V- and a tail-spot; this point, however, I have not carefully studied. No hooked cephalic prepuce can be made out. Its movements also differ from those of filaria nocturna, for it not only wriggles about, just as that parasite does, but it indulges from time to time in long excursions through the blood, moving freely all over the slide, "locomoting," in fact, very much in the same way as filaria nocturna does in the mosquito's stomach after it has cast its sheath.

Parental form and pathology.—The parental form and the life-history of filaria perstans are quite unknown. What pathological rôle it may play is still uncertain. I have conjectured, for reasons stated elsewhere (p. 255), that it may in some way be the cause of negro lethargy and of one of the forms of African craw-craw (p. 520).

FILARIA MAGALHÃESI.

Professor Magalhães describes (*Rev. des Cursos theoricos e prat. da Fac. de Med. de R. de Janeiro*, No. 3, An. III., 1886) two sexually mature filarial hæmatozoa, male and female, which were found lying in the left ventricle of the heart of a child who died in Rio de Janeiro. No information was received as to the nature of the disease of which the child died, nor had any examination of the blood been made during life. The parasites were cylindrical, capillary, opalescent, white, uniform in thickness except where the body tapered towards the tail and at the club-shaped oral end. The mouth was simple, circular, unarmed; the cuticle marked with fine transparent striations. The female worm measured 155 mm. in length by 7 mm. in diameter, the male 83 mm. in length by 4 mm. in diameter. The tail of the latter was provided with four pairs of pre-anal and four pairs of post-anal papillæ, and two spicules. Manifestly this parasite is specifically distinct from filaria Bancrofti. The fact that it occurred in the Western hemisphere would suggest the possibility that it may be the parental form either of filaria Demarquaii or of filaria Ozzardi. Nothing is known of its life-history, nor of the associated pathology.

CHAPTER XXXII.

ENDEMIC HÆMATURIA (BILHARZIA DISEASE).

Definition.—A form of hæmaturia caused by bilharzia hæmatobia (distomum hæmatobium), and characterised by the presence of the ova of that parasite in the urine.

History and geographical distribution.—The frequency of hæmaturia in the natives of Egypt, and in visitors to that country, has long been remarked. The explanation of this peculiar circumstance was supplied by Bilharz, who, in 1851, discovered the cause in a peculiar trematode, subsequently named by Cobbold, in honour of its discoverer, Bilharzia hæmatobia.

The geographical distribution of this parasite is limited to Africa and its island dependencies. Dr. John Harley discovered, in 1864, the characteristic ova in cases of hæmaturia from Natal. It has many times been found in patients from Mauritius. It has been found on the Gold Coast, in Tunis, and it probably exists in many other parts of Africa, more particularly along the eastern side of the continent. Egypt, however, is its favourite haunt; there, judging from Bilharz's, Griesinger's, and Sonsino's *post mortem* records, it is present in quite one-half of the population.

Ætiology.—*The parasite* (Fig. 54).—Bilharzia hæmatobia belongs to the distomidæ; but, unlike the majority of distomes, which are nearly all of them hermaphrodite, bilharzia presents the peculiarity of being bisexual. The *male* is white, cylindroid, measuring 15 mm. in length by 1 mm. in breadth. It possesses an oral and a ventral sucker placed close together.

The cylindrical appearance of the worm is produced by the lateral infolding of the two sides of what would otherwise be a flat body. By this infolding a gynæcophoric canal is formed, in which the female is partially enclosed. The *female* is rather darker in colour than the male, considerably longer (20 mm.), more filiform, her middle being embraced by the gynæcophoric canal referred to, whilst her anterior and posterior portions remain free. The genital openings of the sexes face each other, and are placed immediately posterior to the ventral sucker.

Fig. 54. Bilharzia hæmatobia, male and female, the latter in the gynæcophoric canal of the former. (*After Leuckart.*)

These parasites are found in the blood of the portal vein, in its mesenteric and splenic branches, and in the vesical, uterine, and hæmorrhoidal veins. They have also been found in the vena cava; Sonsino considers that, if searched for, they would probably be found elsewhere in the circulation. Their numbers vary considerably. Sonsino reports finding in one case forty, in another case Kartulis found 300 in the portal vein and its branches.

The ovum (Fig. 55). On microscopical examination, the uterus of the female bilharzia is found to be stuffed with ova of a peculiar and characteristic shape. They are oval, each egg on an average measuring about 0·16 mm. in length by 0·06 mm. in breadth, one end of the ovum being provided with a short, stout, and very definite spine. In certain instances, hereafter to be mentioned, this spine is not terminal but is placed laterally

The exact nature of the process by which the ova leave the body of the human host has not been satisfactorily explained. Apparently, the female worm migrates from time to time from the larger veins to their smaller radicles, and in these deposits her ova. The walls of the bladder and rectum are the favourite situations for this purpose. Afterwards the eggs are somehow carried, possibly aided by the spine with which they are provided, towards the surface of the mucous membrane, and then, falling into the lumen of the bowel or into the bladder, are voided in the fæces or urine, a certain amount of blood escaping at the same time.

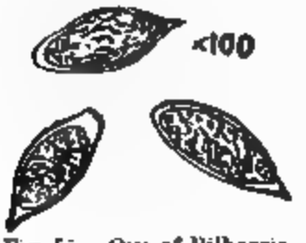

Fig. 55.—Ova of Bilharzia.

The free embryo (Fig. 56).—In newly voided urine the ovum presents a somewhat brownish appearance, and generally contains a ciliated embryo. After a time the embryo may escape through a longitudinal rupture in the shell. It then swims about; but, unless supplied with fresh water, soon perishes. If, however, the urine be freely diluted with water, the embryo not only escapes more quickly from the shell but also continues to live, swimming and gyrating about very actively for a considerable time. While swimming, the body of the little animal undergoes many changes of shape. For the most part, when advancing, it is oblong, tapering somewhat posteriorly; when more stationary it tends to assume a circular form. It moves by means of the cilia which, with the exception of the minute papillary beak, thickly cover the entire body. On carefully examining the embryo, a canal may be traced from the beak into what looks like a rudimentary stomach; on both sides of this two much smaller gland-like organs can be seen,

Fig. 56.—Free embryo of Bilharzia.

and from each of these a delicate tube passes forward and opens, apparently, somewhere in the neighbourhood of the beak. The bulk of the embryo is occupied by a number of sarcode globules. A careful description of the embryo is given by Dr. G. S. Brock in the *Lancet* of Sept. 9th, 1893, p. 625, to which the reader is referred for further details.

Life-history.—Beyond its first stage of free swimming ciliated embryo the extra-corporeal life of bilharzia is quite unknown, notwithstanding the many attempts that have been made to trace its future progress. Sonsino believed at one time that he had discovered its intermediate host in a fresh water arthropode; this view he afterwards abandoned. Judging from analogy, the embryo bilharzia probably passes into the body of some fresh-water mollusc, into some crustacean, or into some larval arthropode; there, it is conjectured, it undergoes the developmental changes into redia and cercaria usually exhibited by the distomes. Later, it probably becomes encysted and then, either free or still in the body of the intermediate host, it gains access to man in drinking water and so, through the stomach, passes to the veins of the portal system.

Symptoms.—The symptoms produced by bilharzia vary in degree within very wide limits. Sometimes the patient experiences no trouble whatever; in other instances the suffering is very great. Indirectly, from the serious nature of the lesions of the urinary organs to which it may give rise, bilharzia is not an infrequent cause of death.

The most characteristic symptom of its presence in the wall of the bladder is the passage of blood at the end of micturition, with or without a sense of urinary irritation. The amount of blood so passed varies from a few drops of slightly tinged urine, to a considerable quantity of pure blood. The quantity of blood passed and the degree of irritation are increased by exercise, by dietetic indiscretions, and by all such causes as are calculated to aggravate cystitis. As a

rule, it is only the last few drops of urine that contain blood; sometimes, however, the hæmorrhage is more extensive, and then the entire bulk of the urine may be blood tinged. Occasionally, clots even are passed.

If in a case of moderate bilharzia infection the urine be passed into a glass and held up to the light, minute flocculi, or coiled up mucoid looking threads will be seen floating about in the fluid. If it be allowed to stand, the flocculi, and perhaps minute clots, will subside to the bottom of the vessel; these, on being taken up with a pipette and placed under the microscope, will be found to contain, besides blood corpuscles and the usual catarrhal products, large numbers of the characteristic spined ova.

In doubtful cases, where ova are few, the best way to find them is to get the patient to empty the bladder and to catch in a watch-glass the last few drops of urine which the patient can force out by straining; these invariably contain ova. A low power of the microscope suffices and is best for diagnosis.

Endemic hæmaturia lasts for months or years. Recovery is rarely complete. In ordinary cases, provided no reinfection take place, the hæmaturia tends to decrease, although ova may continue for years to be found in the last few drops of urine passed. In severe cases, sooner or later, signs of cystitis supervene, and give rise to a great deal of suffering. Not infrequently the ova become the nuclei for stone, and then, of course, the symptoms are those of urinary calculus. Sometimes the pathological changes induced by the presence of the parasite in the bladder lead to the development of new growth, in which event the symptoms become more urgent and the hæmaturia perhaps excessive. Hypertrophy, contraction, or even dilatation of the bladder, are not unusual. Besides the bladder symptoms there may be signs of prostatic disease, or of disease of the vesiculæ seminales causing spermatorrhœa. In the latter case, ova may be detected in the semen. In other instances the ureters and kidneys become involved, and grave disease of

these organs ultimately ensues. In consequence of the continued suffering which these aggravated forms of infection produce, the patients become anæmic, wasted, debilitated, and a ready prey to any intercurrent disease.

When the rectum is involved, dysenteric-like symptoms may supervene, mucus with blood being passed from time to time, the stools becoming frequent and their passage being attended with tenesmus. In such cases small, soft growths are to be felt inside the sphincter ani. On removing one of these and breaking it up with needles, the spined ova can be readily made out in the débris.

In the female, vaginitis and cervicitis have been known to be produced by this parasite. The ova have also been found in the liver and in the lungs; but, so far as known, their presence in the latter organs gives rise to no active symptoms.

Pathological anatomy.—The character of the changes brought about by bilharzia varies very much according to the degree and the duration of the infection. In almost every case the walls of the urinary bladder are early affected. All that may be apparent to the naked eye at this stage of the disease is a certain amount of injection of the small vessels of the mucosa vesicæ, and, according to Sonsino, certain exceedingly minute vesicular or papular elevations of the surface of this membrane. When these minute elevations are examined microscopically they are found to contain ova. Ova are also to be found in the dilated minute blood-vessels. Later, especially in the trigone of the bladder, there are found rounded patches of inflammatory thickening which project somewhat, are granular on the surface and dense in consistence; on section they creak under the knife as if they contained many gritty particles. It is evident that these elevated, thickened patches are the result of an inflammatory process provoked by the clusters of ova which the microscope reveals scattered throughout their entire extent. The ova are principally

deposited in the submucosa, less extensively in the mucous membrane itself, still less in the muscular walls of the organ or in its sub-serous connective tissue. They tend to occur in groups, each of which is invested by a sort of connective tissue capsule; or they may be lying in small blood-vessels which they occlude. Some ova are seen to have undergone calcification; others are still fresh, either segmenting, or already containing a ciliated embryo. On the surface of the rounded patches, already mentioned, phosphatic deposits, also containing ova, are not uncommon; sometimes the patches present minute sloughs. In addition to these indurated patches, various forms of polypoid excrescence—sometimes ulcerated · may protrude from the mucous surface into the cavity of the bladder These various hyperplasiæ frequently contain the adult parasite as well as ova.

In addition to what may be called the specific changes in the mucosa, the muscular coats of the bladder are generally hypertrophied. In consequence of this, as well as of the ingrowth of villosities and different forms of new growth, the capacity of the organ may be much diminished. Its mucous surface is generally coated with a sanguineous mucus containing myriads of ova. Gravel or small stones are sometimes found either imbedded in lacunæ in the hypertrophied and roughened bladder wall, or free in the cavity Not infrequently, a similar hyperplasia occurs in the ureters, particularly towards their lower ends. In rare instances, the pelvis of the kidney itself is affected. Obliteration of the ureter, both from small stones and, also, from thickening of the mucous membrane, has sometimes been met with; it leads to dilatation of the pelvis and atrophy of the parenchyma of the kidney. It is easy to understand how, in time, these changes of the bladder and ureters may give rise to hydronephrosis, pyelitis, abscess of the kidney, and similar secondary affections.

Hyperplasia from bilharzia infection may also occur in the vesiculæ seminales, in the walls of the

vagina, and in the cervix of the uterus, leading to corresponding bloody, ova-containing discharges.

Next to bilharzial infection of the bladder and consequent kidney changes, that occurring in the large intestine, particularly in the lower part of the rectum, is of the greatest practical importance. In this situation polypoid growths, apt to be mistaken for piles, are frequent. Large extravasations of blood under the mucous coat may also occur.

Strange to say, in ova found in the bowel, according to Sonsino and Mackie, the spine is generally placed laterally; whereas in ova coming from the walls of the bladder the spine is invariably terminal. This lateral situation of the spine has been explained in various ways, the most probable suggestion being that it is a consequence of the compression exercised by the muscular coat of the intestine on the parent worm while the ova are passing the shell glands; the relations of certain of the reproductive organs are supposed to be altered by this compression.

It may be mentioned that ova in small numbers have been found in the liver, in gall stones, in the lungs, in the heart, and in the kidneys. We have no knowledge of any definite pathological change entailed by their presence in these organs.

Diagnosis.—The diagnosis of bilharzia disease is easy; the presence of ova in the urine is decisive. In countries like Egypt, where the disease must often concur with chyluria, with stone, with vesical tumour, with gonorrhœal cystitis, and with pyelitis, as well as with prostatic disease, care must be exercised in each particular case to separate the special factors to which the different symptoms are attributable. Thus in chyluria concurring with bilharzia disease there will be chyle in the urine in addition to blood; in such a combination the clot which forms will be large, will contain oil granules and globules and, very probably, filaria embryos in addition to bilharzia ova; moreover, the filaria will generally be detectable in the finger

blood if looked for at night. Stone in the bladder, when suspected, has to be searched for with the sound. In gonorrhœal cystitis the history of gonorrhœa will be forthcoming In prostatic disease, enlargement of this organ may be made out; and so on. Difficulty may sometimes arise when ova are few in number, or when they have ceased altogether to come away, the parent worm or worms having died. The mischief wrought by the parasite remains, although the ova —the most certain evidence of the parasite's previous presence -may be discharged no longer. But, even if ova are very few, they may still be found in the last drop or two of urine passed, as has been mentioned. If they are no longer to be found in the urine, sometimes, by scratching the surface of the bladder with a sound and examining the shreds of mucus so obtained, a few, calcified it may be, but presenting the characteristic spine, may be seen with the microscope. In rectal disease, if bilharzia be suspected, the mucus and the fæces, or, failing these, one of the polypoid growths after removal by finger or forceps, as well as the urine, should be examined for ova.

Prognosis.—An important element to be considered in venturing on a prognosis is the long life of the parasite. Sonsino mentions a case in which living ova were still being passed nine years after their first appearance, and after all chance of reinfection had ceased. Another important element in prognosis is the degree of infection; the greater the number of worms the more severe and the more extensive the disease they produce. As with filarial infection, the greater the number of cases in a district the greater will be the probability of severe infections being met with. The prognosis is practically that of a chronic cystitis depending on an irremediable, but not in itself fatal, cause. Much suffering may often be looked for and, as a consequence, anæmia and debility; possibly calculus may be formed, possibly grave renal disease may ensue. In the milder degrees of infection, which

fortunately are the commonest, the patient seems to be in no way inconvenienced by the parasite, and generally escapes all serious consequences. In any case, mild or severe, there may be attacks of hæmaturia from time to time; as a rule, the quantity of blood lost is insignificant.

Treatment.—Our knowledge of the situations occupied by the parasite indicates the futility of attempting a radical cure by means of poisonous substances, whether introduced by the bladder, by the rectum, or by the stomach. As yet, we know of no direct, or other, means by which the bilharzia can be destroyed. Harm only can result from attempts at a radical cure of endemic hæmaturia on such lines. Our efforts must, therefore, be confined to palliating the effects of the presence of the parasite. Practically, the treatment resolves itself into that of chronic cystitis. The diet should be bland, but fairly nutritious; stimulants and spices are to be avoided. Excess of all kinds, violent muscular efforts, cold and other causes of catarrh must also be guarded against. During exacerbations of hæmaturia, or of cystitis, rest should be enjoined and diluents freely partaken of. Pain may demand anodynes. Excessive catarrh of the bladder suggests washing out with weak boric acid lotion, and the internal administration of uva ursi, buchu, perhaps small doses of cubebs, copaiba, or sandalwood oil, salol, benzoic acid, and so forth. Stone, and troublesome new growths, are to be removed by operation. Where distress is extreme, Mackie has had good results from cystotomy. Polypoid growths in the rectum, where accessible, should be removed. Hyperplasia in the vagina and cervix are best treated by scraping.

Prevention.—Since analogy justifies the belief that the embryo of bilharzia, on obtaining access to fresh water, enters a fresh-water animal and by it obtains access to another human host, it is evident that if the embryo be kept from getting into the water, or, if drinking water be boiled or filtered, the

is reputed to attain in some instances enormous dimensions; it is probable, however, that worms of five or six feet in length owe their size to errors of observation, two worms, or their fragments, having been regarded as one. According to Ewart, in forty carefully measured specimens, the shortest was 12¾ inches, the largest 40 inches in length, 30 inches is probably an average length. The diameter of the worm is about one-tenth of an inch. The body is cylindrical, milky-white, smooth, and without markings. The tip of the tail is abruptly bent, forming a sort of blunted hook, perhaps functioning as a "holdfast." The head end is rounded off, terminating in what is known as the cephalic shield. The mouth is triangular, very small, and surrounded by six papillæ—two large and four small. The alimentary canal is relatively small, being compressed and thrust to one side by the uterus; it is probably cæcal, for it has not been traced to an anus. The vagina, which must have existed at an early stage, at maturity has also become obliterated by the growth of the enormous uterus which, filled with coiled-up embryos (Fig. 58), extends from the head to the tail of the worm.

Fig. 57. Guinea worm. (Reduced.) (*Leuckart.*)

Habits.—The habitat of the female guinea worm is the connective tissue of the limbs and trunk. When mature, in obedience to instinct, she proceeds to bore her way through this tissue, and, finally, travelling downwards, reaches a leg or foot. In 85 per cent. of cases she presents in some part of the lower extremities; occasionally in the scrotum; rarely in the arms; very

exceptionally in other parts of the body, or even in the head. Arrived at her destination she pierces the derma. Probably in consequence of some irritating secretion, a small blister now forms and elevates the

Fig. 58.—Section of guinea worm. (*Leuckart.*)

epidermis over the site of the hole in the derma. By-and by the blister ruptures, disclosing a small superficial ulcer half to three-quarters of an inch in diameter. At the centre of the ulcer, which sometimes quickly heals spontaneously, a minute hole, large enough to admit an ordinary probe, can be seen. Sometimes when the blister ruptures the head of the worm is seen protruding from this hole; as a rule, however, at first the worm does not show herself. If now we douche the neighbourhood of the ulcer with a stream of cold water expressed from a sponge and, as the water falls, watch the little hole in the centre of the ulcer, we shall see in a few seconds a droplet of fluid -at first clear, later milky well up through the hole and flow over the ulcer. Sometimes, instead of this fluid, a small, beautifully pellucid tube, about $\frac{1}{70}$ of an inch in diameter, doubtless the uterus of the worm prolapsed through her mouth, is projected

through the hole in response to the stimulus of the cold water. When this tube has been extruded an inch or thereabouts, it suddenly fills with an opaque whitish material, ruptures and collapses, the fluid

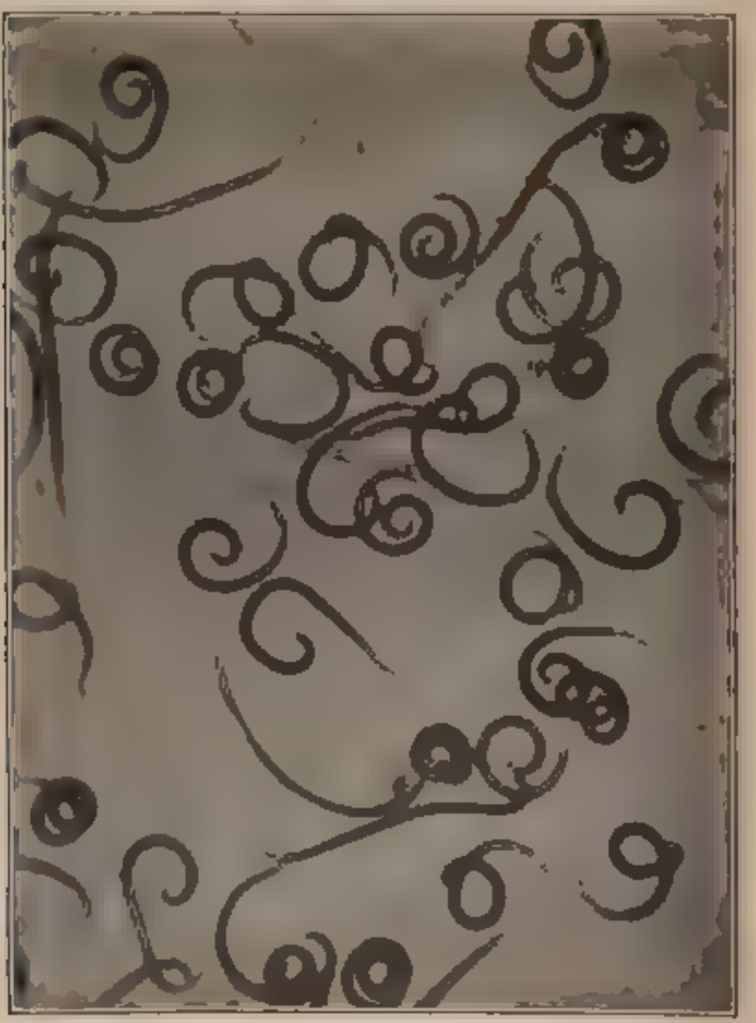

Fig. 70. Embryos of guinea worm
(*From a photogram by Mr. H. B. Bristow.*)

spreading over the surface of the ulcer. If a little of the fluid, either that which has welled up through the hole, or that which has escaped from the ruptured tube, is placed under the microscope, it is seen to contain myriads of embryo guinea worms lying coiled up, almost motionless, with their tails projecting

in a very characteristic manner (Fig. 59). If now a drop of water be instilled below the cover-glass the embryos may be observed to unroll themselves and, in a very short time, to swim about, *more suo*, with great activity. Manifestly these embryos come from a guinea worm lying in a tissues and communicating with the surface through the little hole in the derma.

The embryo (Fig. 60).—The embryos are not cylindrical; they are distinctly flattened. In swimming they move by a sort of side to side lashing of the tail, and tadpole-like motion of the body. The movements are intermittent; sudden, short swims alternating with brief pauses. When progressing the longer transverse axis of the body is perpendicular to the plane travelled over; but when, from time to time, the little worms pause they gradually roll over on to their flat surfaces. As soon as they come to rest on the flat they suddenly recover themselves with a jerk, and turn quickly on to their edges and begin swimming about again. This series of movements is constantly repeated.

The embryo of the guinea worm measures about $\frac{1}{30}$ of an inch in length, by $\frac{1}{1000}$ of an inch at its greatest breadth. The head is somewhat tapered and then abruptly rounded off. The tail is long, slender, and sharp-pointed. The alimentary canal can be readily detected. Towards the root of the tail two

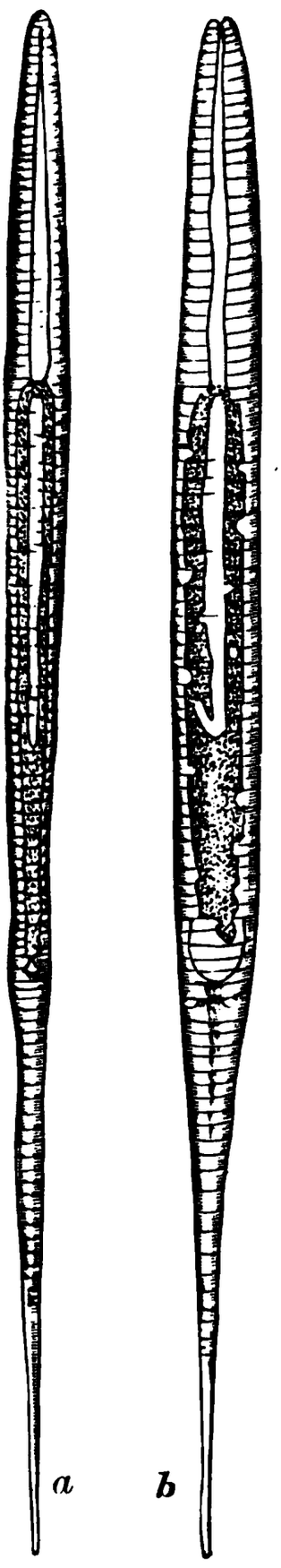

Fig. 60.—Embryos of guinea worm.
a, Side view; *b*, front view. (× 250.)

peculiar gland like organs, placed opposite to each other, can be made out. The cuticle is very distinctly transversely striated.

In clean water the embryo remains alive for six days; in muddy water, or in moist earth, it will

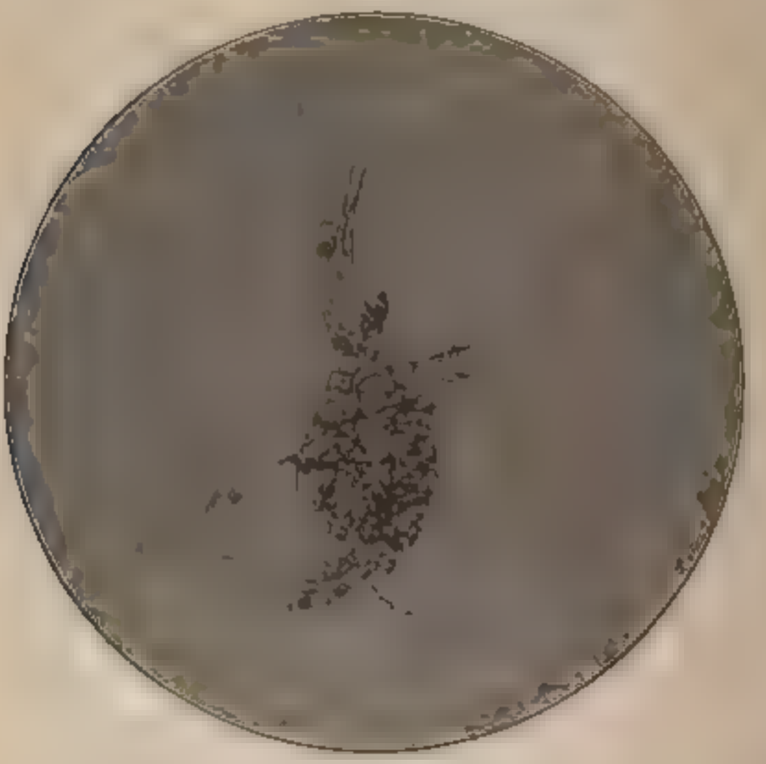

Fig. 61 Embryos of guinea worm in body-cavity of cyclops. The cyclops has been slightly compressed so as to force out some of the worms, which can be seen escaping from ruptures at the head and tail (*From a photogram by Mr. Andrew Pringle.*)

live from two to three weeks. If slowly desiccated it does not die; it may be resuscitated by placing it again in a little water.

Intermediate host. If, by way of experiment, we place some guinea worm embryos along with cyclops quadricornis in a watch-glass we shall find that, after a few hours, the embryos have transferred themselves to the interior of the body-cavity of the cyclops, where

they can be seen moving about, coiling and uncoiling themselves, with great activity (Fig. 61). As many as fifteen or twenty young guinea worms may be counted in each of the little crustaceans, which, unless the infection is excessive, seem in no way inconvenienced. After a time, the embryos so transferred undergo a metamorphosis. They cast their skins two or three times, get rid of their long swimming tails, acquire a cylindrical shape and, ultimately, along with increased size, develop a tripartite arrangement of the extreme posterior end, which recalls a similar arrangement in the tail of filaria nocturna towards the termination of that nematode in the mosquito.

Mode of infection.—The metamorphosis of guinea worm in cyclops was discovered by Fedschenko in Turkestan. His observations I have been able to confirm in England; but, in the colder climate of the latter country, in English cyclops the metamorphosis takes somewhat longer to complete; eight or nine weeks, instead of five weeks as in Turkestan. Fedschenko supposed that the cyclops containing the embryo guinea worm, on being swallowed by man in drinking water, was digested; and that the parasite, being then set free, worked its way into the tissues of its new and definitive host. It is possible, however, that the embryo may have to undergo further changes before it is fitted for life in man. Considering the peculiar geographical limitations of this helminthiasis, and the very general distribution of cyclops, such an arrangement seems likely enough. However this may be, Fedschenko's discovery makes it certain that it is in drinking water that the guinea worm is acquired.

The male worm.—Nothing certain is known, as already stated, about the male worm; nor as to when or where impregnation of the female is effected. Impregnation probably occurs at an early stage of parasitic life, and long before the female worm has grown to the great length which she subsequently attains. The male worm, his function fulfilled, probably dies and is absorbed.

Biological peculiarities explained.—The little we now know of the life-history of the guinea worm explains many things that were formerly mysterious. We now understand why the parasite, on attaining maturity, makes for the legs and feet; these are the parts of the human body most likely, in tropical countries, to come in contact with puddles of water, the medium in which cyclops—the intermediate host—lives. We can understand, also, why it is that the contact of water with the skin of the host causes the guinea worm to extrude her young; and we can understand the rationale of the douching, so much practised by the natives of certain of the endemic districts, in their attempts at extraction.

Premature death of parasite.—Occasionally the guinea worm fails to pierce the integument of her host; sometimes she dies before arriving at maturity. In either case she may give rise to abscess; or she may become cretified, and in this condition may be felt, years afterwards, as a hard convoluted cord under the skin of the leg, or be discovered only on dissection.

Treatment.—Formerly it was the custom, so soon as a guinea worm showed herself, to attach the protruding part to a piece of wood and endeavour to wind her out by making a turn or two of this daily. Sometimes these attempts succeeded; but, just as often, the worm snapped under the strain. The consequences of this accident were often disastrous. Myriads of young escaped from the ruptured ends into the tissues, and violent inflammation and fever, followed by abscess and sloughing, ensued; weeks, or months, perhaps, elapsed before the unhappy victims of this rough surgery were able to get about. Too often serious contractions and ankyloses, from loss of tissue and inflammation, and even death from septic trouble, resulted.

If a guinea worm be protected from injury, and the part she occupies frequently douched with water, her uterus will be gradually and naturally emptied of embryos. Until this process is completed she resists extraction; possibly the hook at the end of her tail

assists her to maintain her hold. But when parturition, in from fifteen to twenty days, is completed, the worm tends to emerge spontaneously. A little traction or winding out if practised then may aid extrusion. Traction, however, must not be employed so long as the embryos are being emitted. The completion of parturition can be easily ascertained by the douching experiment already described.

Lately Emily, a French naval surgeon, has introduced a system of managing guinea worm cases which bids fair to shorten treatment and obviate the serious risks of the old winding out system. By means of a Pravaz's syringe he injects the body of the worm, if she chances to be protruding, with solution of bichloride of mercury, 1 in 1,000. This kills the parasite ; after twenty-four hours, extraction is generally easily effected. If the worm has not shown herself externally, but can be felt coiled up under the skin, he injects as near the coil as possible, and through several punctures, a few drops of the same solution. This, too, kills the parasite. Her body is then absorbed, as a piece of aseptic catgut would be, without inflammation or reaction of any description ; or she may be cut down on, and easily extracted. Others have confirmed the value of Emily's method, which saves much time and suffering and with due care is devoid of risk.

FILARIA LOA (Fig. 62).

This parasite is peculiar to the West Coast of Africa where, in many parts, it is not uncommon—in Old Calabar, for example. The male worm measures about 25 to 30 mm. in length by 0·3 mm. in breadth, the female 30 to 40 mm. in length by 0·5 mm. in breadth. Both sexes are filiform, cylindrical, colourless, like fine fishing gut, tapering slightly at the head, more decidedly at the tail. The body is dotted over with minute chitinous bosses. The anus is subterminal. The

Fig. 62.—Filaria loa. (Nat. size.) (*Dr. Argyll Robertson.*)

tail of the male (Fig. 63) is markedly incurvated and provided with five large papillæ on each side of the anus, and two rather short, unequal spicules. The mouth is simple, punctiform, and without armature.

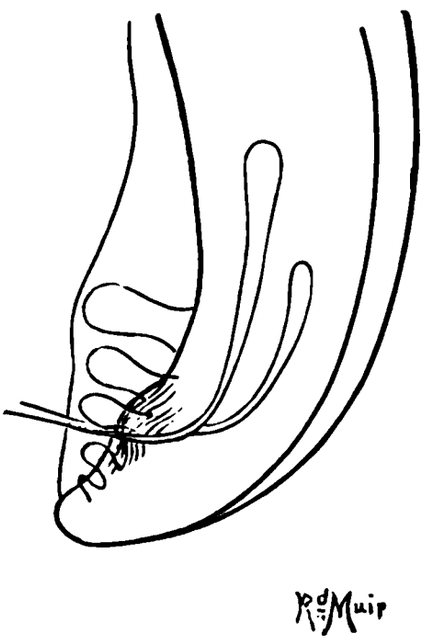

Fig. 63.—Tail of male filaria loa.

The habitat of filaria loa appears to be the subcutaneous connective tissue, which it traverses freely. When, in the course of its wanderings, it crosses the subconjunctival connective tissue, and the delicate integuments about the orbit, it becomes distinctly visible. When passing under such thin structures as the skin of the eyelids, or that over the bridge of the nose, or when moving about under the skin of the fingers, the slight elevations it gives rise to, as well as its movements, are sometimes appreciable, and may be both seen and felt.

From the circumstance that this parasite has occasionally been seen in individuals who have been ten or more years away from the endemic area in which alone it can be contracted, we may conclude that the loa is long-lived.

The female produces sheathed embryos closely resembling filaria nocturna and filaria diurna. At one time I had a negro patient under my care in whose blood filaria diurna abounded. This man remembered that, when a lad, he had a loa in his eye. I have thought, therefore, that filaria diurna may be the embryonic form of filaria loa. On the other hand, Dr. Argyll Robertson has placed on record a remarkable case of filaria loa in which the parasites, a male and a pregnant female were removed from the eye. The patient's blood was frequently examined, but no embryos were found. Lately I had an opportunity of examining the blood of another patient known to

be the subject of loa infection, but failed to find any hæmatozoal embryos. We do not know in what way the embryo escapes from the human body, nor do we know anything about its life history outside the human body. Notwithstanding the failures to find the embryo in the peripheral blood, analogy suggests that it probably circulates for a time in this fluid and, like filaria nocturna, that it is removed from this medium by some suctorial insect which acts as intermediate host.

Filaria loa, as stated, is very active in wandering about the body, but it seems to have a predilection for the eyes and neighbourhood. It comes and goes there at irregular intervals of days, weeks, or months, traversing the subconjunctival tissue, and moving across the bridge of the nose from one eye to another. Warmth seems to solicit its presence near the surface. The sexes appear to hunt each other about; at all events, in Dr. Argyll Robertson's case (*Trans. of the Ophthalmalogical Soc.*, 1895) a male worm was removed from the eye, and not long afterwards a female worm appeared about the same situation and was also removed.

The worm gives rise to pricking, itching, creeping sensations and, occasionally, transient œdematous swellings in different parts of the body. When it appears under the conjunctiva, it may cause a considerable amount of irritation and congestion. There may be actual pain even, associated with swelling and inability to use the eye and, perhaps, tumefaction of the eyelids.

Treatment.—The negroes treat filaria loa in two ways—either by dropping a grain of common salt into the conjunctival sac, which has the effect of driving the filaria away, for a time at least; or they extract it with a sharp thorn, or by some other rude surgical means. With proper instruments there is no difficulty in removing the parasite from under the conjunctiva or from the eyelid—that is, if the operator is possessed of

the requisite deftness in operating. All that is necessary, on the parasite showing itself, is, after cocainising the eye, to seize the conjunctiva with a pair of forceps, taking care to include the worm and the subconjunctival connective tissue in the grasp of the instrument. Having fixed the parasite in this way, the conjunctiva may be snipped through with scissors; when, with the aid of another pair of forceps, and after releasing the first pair, the parasite may be withdrawn. In the case of the parasite showing itself elsewhere, I would suggest that it might be killed, as in the case of the guinea worm, by local hypodermic injection of bichloride of mercury solution (1 in 1,000).

FILARIA VOLVULUS.

A medical missionary transmitted to Professor Leuckart two tumours, the size of a pigeon's egg, which had been removed, one from the scalp, the other from the chest, of Gold Coast negroes. Each of the tumours contained several male and female filariæ, the former 60 to 70 centimetres, the latter 30 to 35 centimetres in length. The worms were coiled up in the form of a ball, and were bathed in a fluid full of embryos resembling filaria nocturna and filaria diurna; no sheath, however, was visible. Nothing further is known of these parasites and the diseases, if any, to which they may give rise.

CRAW-CRAW.

Most itching papular and pustular eruptions are termed kra-kra by the natives of the West Coast of Africa. Dr. John O'Neil describes (*Lancet*, Feb., 1875) under this name a pustular affection which he says is common in certain parts of the West Coast, and which he found to be associated with the presence of a filariform parasite in the papules. O'Neil says that this form of craw-craw resembles scabies; but he adds that symptoms subside in a cooler climate, to return, however, when the negro revisits the hot and damp atmosphere of his native country.

The papules occur all over the limbs and body, either singly or in rings. In two days from its appearance the papule, he says, becomes a vesicle, and in two more a pustule.

On paring off the top of the papule with a sharp knife, and teasing up the little piece of integument in water, he found a number of minute filaria-like organisms wriggling about with great activity. Their activity speedily slowed down, and in a short time the worms died. These organisms, according to O'Neil's drawings and description, resemble somewhat filaria nocturna. The measurements do not quite correspond however, the craw-craw filaria being shorter and broader ($\frac{1}{100}$ inch by $\frac{1}{2000}$ inch) than filaria nocturna; moreover, unlike the latter, it presented two black markings at the cephalic end. He says that if the section of the papule be made sufficiently deep, five or six of these parasites may be seen in a field.

Craw-craw is said to be contagious. It appears after an incubation period of three days, and is incurable by sulphur inunction.

O'Neil's observations have not been confirmed. I think it is quite possible that the parasite he found was one of the blood filariæ we now know to be so common on the West Coast of Africa. It is comprehensible that in a country in which filaria perstans occurs in every second individual, it would be frequently found in such preparations as Dr. John O'Neil examined. The removal of the top of a scabies papule would certainly be attended with some degree of hæmorrhage; in which case, should the patient chance to be the subject of any form of filaria infection, these parasites would be found in the preparation. I do not wish to assert that O'Neil's parasite was filaria perstans, but the possibility of this must not be overlooked. A disease resembling O'Neil's craw-craw was described some time ago (*Archives de Méd.*, April, 1882) by Prof. Nielly under the title "dermatose

parasitaire." A French lad, who had never been abroad, became affected with a papulo-vesicular itching eruption resembling scabies, in which Nielly found a filariform parasite somewhat like that discovered by O'Neil in craw-craw. It had the same peculiar cephalic markings; in addition, it had a well-defined alimentary canal and rudimentary organs of generation. Nielly found nematode embryos in the blood in this case; so that we are justified in believing that the parasite in the skin was an advanced developmental form of the embryo in the blood, and that both were the progeny of a mature parental worm living somewhere in the tissues. Possibly Nielly's dermatose parasitaire and O'Neil's craw-craw were of the same nature. I have suggested that, as the skin parasite in O'Neil's disease may have been an advanced form of filaria perstans, this parasite normally, and in pursuance of its evolution, escapes from the human body through the skin after undergoing there a certain measure of developmental advance. Further investigations on this subject are much wanted.

CHAPTER XXXIV.

III. PARASITES OF THE LUNGS.

ENDEMIC HÆMOPTYSIS: DISTOMUM RINGERI.

(*v. D. Westermanni, v. pulmonale*).

Geographical distribution.—So far as known, this disease is confined to Japan, Corea, and Formosa. In some districts a notable percentage of the population is affected. It is not improbable that, as knowledge extends, the disease will be found to exist in other countries. Recently the parasite which gives rise to this peculiar form of blood spitting has been found in the United States, both in the cat and in the dog. It is not at all unlikely, therefore, that ere long we may hear of endemic hæmoptysis from America. The Chinese and Japanese are nowadays to be found in almost every land, and doubtless they carry with them their peculiar parasites—d. sinense, d. crassum, and also d. Ringeri.

Symptoms.—The subjects of endemic hæmoptysis have a chronic cough, which is usually most urgent in the morning on rising. The fits of coughing eventuate in the expulsion of a peculiar rusty brown, pneumonic-like sputum. This sputum can be produced at will almost at any time and often in considerable quantity. In addition to the chronic cough and the rusty expectoration referred to, the patient is liable to irregular attacks of hæmoptysis; though usually induced by violent exertion, occasionally such attacks come on without apparent cause. The hæmoptysis may be trifling; on the other hand, it may be so profuse as to threaten life—at all events, to cause intense anæmia.

The ovum.—On placing a minute portion of the

viscid, pneumonic-like sputum under the microscope, its peculiar colour is found to be due partly to red blood corpuscles, partly to a crowd of dark brown, thick-shelled, operculated ova (Fig 64). These ova

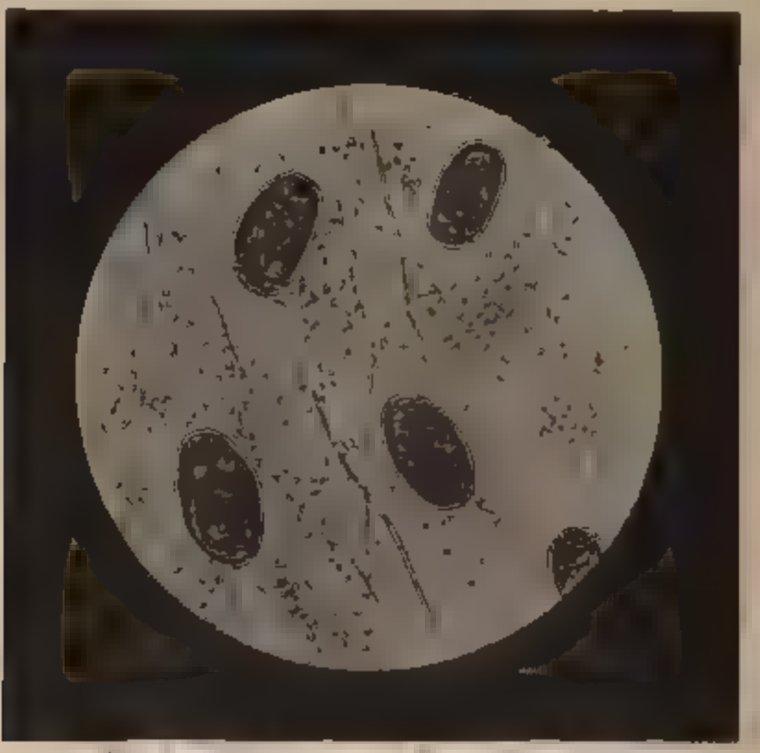

Fig 64.—Ova of distomum Ringeri in sputum.

vary a good deal in size and shape; they are all, however, distinctly oval, smooth, double-outlined, and measure from 80 to 100 μ in length, by 40 to 60 μ in breadth. If the sputum is shaken up in water, and the water be renewed from time to time, in the course of a month or six weeks—longer or shorter according to temperature—a ciliated embryo is developed in each ovum. When the ovum is mature, on placing it on a slide and exercising slight pressure on the cover glass, the operculum is forced back, and the embryo immediately emerges and at once begins to swim and gyrate in the water. Farther than this the life history of this parasite has not been traced; but, doubtless, it is continued in

some fresh-water animal, through which it finds its way back, in a more or less direct way, to man.

Pathological anatomy. On making a section of the lungs in this disease, a larger or smaller number of what are known as "burrows" are discovered scattered about the organ, particularly towards their periphery. These burrows consist of areas, somewhat larger than a filbert, of infiltrated lung tissue, in which can be seen a number of tunnels filled with the same material that constitutes the characteristic sputum, and also containing one, two, or more small distomes. The septa between the tunnels may break down and a considerable cavity be thus produced; and as this occurs in connection with one of the bronchi, with which the tunnels always communicate, it may give rise to the appearance of a dilated bronchus. One burrow may communicate with another.

When first discovered it was supposed that d. Ringeri was confined to the lungs. Later investigation has shown, however, that it may affect the liver, peritoneum, testes, and even the brain. In the latter it forms a sort of tunnelled tumour similar to that in the lungs; and, by the pressure or irritation proceeding from this tumour, may give rise to a peculiar and ultimately fatal form of Jacksonian epilepsy.

Fig. 65. Distoma Ringeri. (*Leuckart.*)

The parasite (Fig. 65). —The parasite itself is reddish brown in colour, thick and fleshy, and oval in form. So thick is it that its transverse section is almost round. It measures 8 to 10 mm. in length by 4 to 6 mm. in breadth, and is covered with minute spines.

Diagnosis.—Diagnosis of endemic hæmoptysis is at once established by the discovery of the characteristic ova in the almost equally characteristic sputum Râles and other physical signs of lung consolidation are not usually discoverable.

In the case of one sided convulsions, or in hemiplegic affections occurring in a native of, or in a visitor from, the countries in which this distome is endemic, the sputum should be examined on the chance of discovering evidence of the parasite. Should ova be found, there is a strong presumption that the cerebral trouble arises from distomum tumour in the brain.

Treatment.—Hitherto no means of expelling this parasite from the lungs has been discovered. In the case of cerebral distomiasis it might be possible by an operation to remove the parasite and associated tumour, and thus afford a chance of recovery in what has hitherto proved a fatal condition.

Prophylaxis in this, as in so many animal parasitic diseases, principally lies in the direction of securing a pure water supply and avoiding all uncooked articles of diet which might be supposed to contain the young parasites.

CHAPTER XXXV.

IV. PARASITES OF THE LIVER.

DISTOMUM CONJUNCTUM.

DISTOMUM CONJUNCTUM (Fig 66, *a c*) was discovered by MacConnell in an East Indian in 1874. It is leaf-shaped, narrower in front than behind, and measures 9 to 12 mm. in length by 2½mm. in breadth. Its surface is covered with minute spines. The eggs (Fig. 66, *b*) are oval, operculated, and measure 34 μ in length by 19 μ in breadth. This parasite inhabits the bile ducts, which it thickens and sacculates. Apparently d. conjunctum is but of slight importance pathologically.

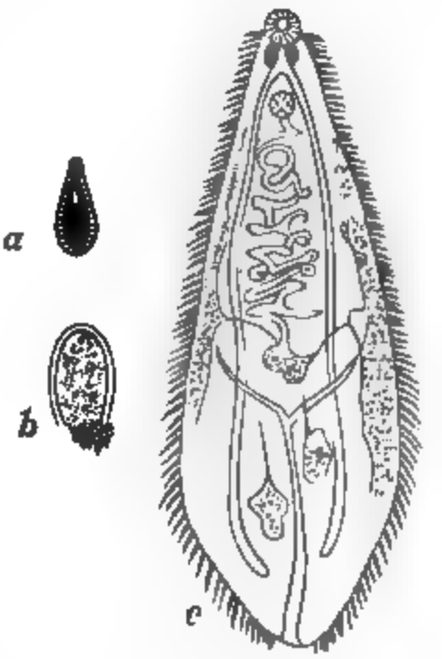

Fig. 66.—Distomum conjunctum.

DISTOMUM SINENSE.

Distomum sinense was discovered almost simultaneously by MacConnell in India and MacGregor in Mauritius, in 1874. It has been found in many Eastern countries, including India, Mauritius, Japan, Corea, Formosa, China, and Tonkin. In the last-named country it appears to be very common.

D. sinense (Fig. 67, *a*, *c*) measures from 20 to 22 mm. in length; it is oblong, narrow, and somewhat pointed anteriorly, reddish in colour, and

almost transparent. The eggs (Fig. 67, *b*) are 28 to 30 μ in length by 16 to 17 μ in breadth, operculated, almost black in colour, and contain a ciliated embryo. Nothing is known of the life-

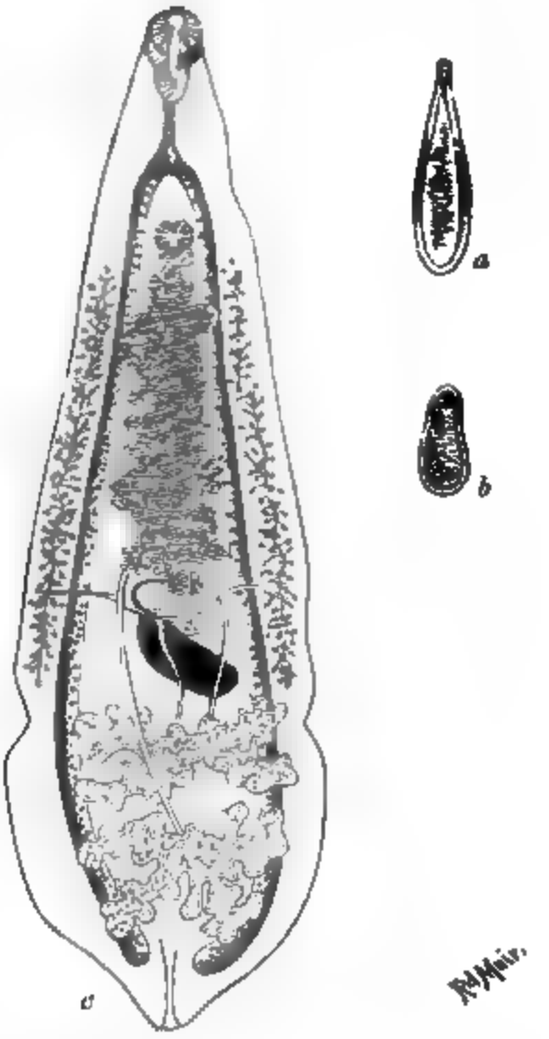

Fig. 67.—Distomum sinense.

history of the parasite farther than that it may occur in some of the lower animals—in the cat, for example. Probably its immature stages are passed in a mollusc or other small, soft-skinned, fresh-water animal.

D. sinense inhabits the bile ducts and gall-bladder. It dilates and thickens the biliary canals, expanding

them in places into cavities and diverticula as large as a filbert. In these cavities vast numbers of parasites are sometimes found. The diverticula communicate with the bile ducts, along which the ova of the parasites, and sometimes the parasites themselves, escape into the intestine. The affected liver is enlarged on the whole, although the tissue in the immediate neighbourhood of the diseased bile ducts is atrophied. The spleen, also, may be hypertrophied, and the intestine in a condition of chronic catarrh.

This parasite, which for long was supposed to be practically innocuous, is now known to be the cause of a serious disease of the liver which may terminate fatally.

Baelz discovered that in certain low-lying, unhygienic villages in Japan this helminthiasis was exceedingly common, quite 20 per cent. of the inhabitants being affected. When the infection is severe the liver becomes enlarged, and chronic diarrhœa, with recurring attacks of jaundice, sets in. Later, anasarca appears, and gradually a cachexia resembling that of sheep rot is established which, in the course of several years, may prove fatal.

It would be well to bear this parasite in mind in approaching the diagnosis of obscure hepatic disease, associated with diarrhœa and jaundice, in patients from the East. It is just possible that the discovery of the ova in the stools might guide to a correct diagnosis.

PENTASTOMUM CONSTRICTUM (Fig. 68).

This, which is probably a formidable parasite, has now been found a number of times encysted in the liver, and occasionally in the lungs, of African negroes. It appears to give rise to a considerable amount of irritation, perhaps to peritonitis and to pneumonia. Nothing is known as to the way in which man becomes infected with the parasite, of which the larval form alone has been recognised.

This is of a milky white colour, from 1 to 1½ inch in length, cylindrical, flattened on the ventral surface, ringed, rounded anteriorly, and terminating posteriorly in a blunt cone. The anterior end is provided with two pairs of hooks arranged on

Fig. 68.—Pentastomum constrictum. (Aitken.)

Fig. 69.—Pentastomum constrictum encysted in the liver. (Aitken.)

either side of the pit-like mouth. The posterior aspect of the rings, twenty-three in number, carries a number of minute spinous projections. The parasites, surrounded by their integumental exuviæ, are found (Fig. 69) each coiled up in a cyst-like pouch, and scattered through the substance of the liver, or projecting as nodules on the surface of the gland. Aitken ("Principles and Practice of Medicine," 4th ed., 1866) gives a very complete account of a case of a negro in which the pentastomum seemed to be the cause of death. He gives a drawing from another case showing the cysts in the liver, from the surface of which one of the parasites is protruding into the peritoneal cavity.

CHAPTER XXXVI.

V. INTESTINAL PARASITES.

NEMATODES.

Microscopical examination of the fæces for ova of intestinal parasites.—If the fæces of the natives of warm climates, and of Europeans coming from warm climates, are systematically examined with the microscope, it is astonishing how frequently they are found to contain the ova of three species of nematode worms—ascaris lumbricoides, trichocephalus dispar, and ankylostomum duodenale. The ova of the tapeworms and of the common threadworm (oxyuris vermicularis), are rarely found in the stools, as these parasites do not, as a rule, part with their ova until the joints of the former, or the entire body of the latter, have left the alimentary canal; but as the three nematodes mentioned pass their eggs directly into the bowel, these eggs habitually appear in the fæces, and constitute unequivocal evidence of the presence of their respective parental forms. Occasionally the ova of the rarer hepatic and intestinal parasites—such as bilharzia hæmatobia, distomum sinense, distomum crassum, distomum hepaticum, and one or two still rarer helminths are encountered; as these, with the exception of bilharzia, are very rare, from a practical point of view they may be disregarded. Without large experience, the ova of the rarer parasites cannot be identified off-hand; but if the practitioner has learned to recognise those of the three common species, he will at once know when he comes across the ova of any of the rarer species and, on referring to some special work on helminthology, will have little difficulty in arriving at a correct diagnosis.

The microscopic examination of fæces for ova, though somewhat disagreeable, is by no means a difficult matter. All that is necessary, by way of preparation, is to place on the slip a minute portion of the suspected fæces—about the size of a hemp seed—and then to apply the cover-glass, gently gliding it over the slip so as to spread out the mass in a thin, fairly uniform, and transparent layer. If the bit of fæces prove too consistent, a little water may be added so as to soften it. If the stools are loose and watery, the sediment should be taken up with a pipette and examined. It is well to make two or three preparations. The microscopic examination must, in the first instance, be made with a low power—an inch, or better, a half-inch objective. Search must be made in every part of the slide, and every suspicious body carefully scrutinised, a higher power being used if necessary. A very little practice suffices for the identification not only of ova but of the species of parasite to which the ova belong.

The points to attend to in the diagnosis of ova are size, shape, colour, thickness, roughness, smoothness, or markings of the surface of the shell; the presence or otherwise of yolk spheres, of a differentiated embryo, or, in the case of the tæniæ, of the three pairs of embryonic hooklets; the existence of an operculum in the case of certain distomes and of bothriocephalus. The ova of the same species of parasite vary but slightly, and are in every instance sufficiently stable and definite for correct diagnosis.

Ova of trichocephalus dispar (Fig. 70, *a*).—Of the three common nematodes mentioned—trichocephalus dispar, ascaris lumbricoides, and ankylostomum duodenale—the ova of the first are those most frequently met with. They occur sometimes in enormous numbers, as many as six or eight specimens being visible in one field of an inch objective. They form rather a striking object under the microscope. They are oval, measuring from 56 μ by 24 μ to 36 μ by 26 μ, the ends of the long axis of the oval being slightly pointed and tipped

with a little shining projection or plug. Their general appearance suggests an elongated oval tray, the projections at the poles of the ovum representing the handles of the tray. They are dark brown in colour, sharply defined, double outlined, and contain no differentiated embryo.

The *ova of ascaris lumbricoides* (Fig. 70, *b*) are considerably larger (60 to 75 μ by 36 to 55 μ) than those of the trichocephalus dispar. They are also, as a rule,

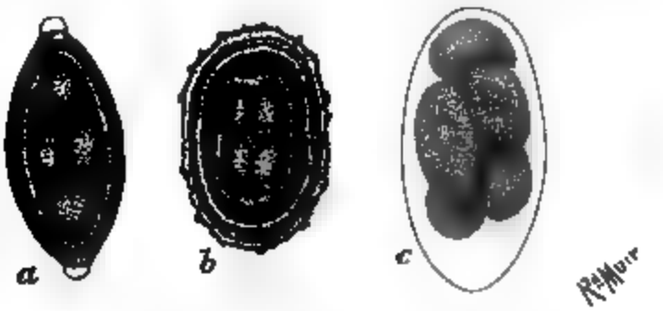

Fig. 70.—*a*, trichocephalus dispar; *b*, ascaris lumbricoides; *c*, ankylostomum duodenale. (*Sonsino.*)

more spherical or, rather, more broadly oval; occasionally they are almost barrel-shaped. Like those of trichocephalus, they are dark brown in colour from bile staining, but they are much less sharply and smoothly defined, possessing a coarse thick shell which is roughened by many warty excrescences. The yolk contents are not always easily made out, nor, when made out, can any sign of embryo or segmentation be discovered.

The *ova of ankylostomum duodenale* (Fig. 70, *c*) contrast very markedly with both the foregoing, particularly in the matter of colour. Trichocephalus and ascaris ova are invariably dark and bile-stained; those of the ankylostomum are beautifully clear and transparent. They measure 55 to 65 μ by 32 to 43 μ; have a regular, somewhat elongated oval form, with a delicate, smooth, transparent shell through which two or four light grey yolk segments can be distinctly seen. It is well to search for these ova soon after

the fæces have been passed, otherwise, owing to the rapidity with which, in favourable circumstances, development proceeds, the embryo may have quitted the shell and the egg be no longer visible.

Trichocephalus dispar.

Trichocephalus dispar, or the whip-worm, lives principally in the cæcum. In many countries it is present in more than half the population Further than that the practitioner should be familiar with the appearance of its eggs in the stool, so that he may be able to distinguish them from those of ascaris, of ankylostomum, and of other parasites, its presence is of no practical moment. So far as known, it gives rise to no serious pathological lesion; a fortunate circumstance, seeing that hitherto it has been found impossible, with any degree of certainty, to dislodge it by anthelmintics.

Ascaris lumbricoides.

Though not quite so common in tropical countries as trichocephalus, the ascaris is nevertheless very common indeed, especially in children, who often harbour these loathsome creatures in enormous numbers—in dozens, or even in hundreds. In those countries, at one time or another, nearly every child gets them; so much so that, when doubt exists about the nature of some obscure affection, a dose or two of santonin often produces results which will seem to justify a diagnosis of "worms," and, for the time being perhaps, satisfy an anxious mother.

Mode of infection.—The reason for the great frequency of ascaris lumbricoides in tropical countries is probably twofold—the warmth of the climate, and the habits of the people with regard to the disposal of night-soil. In the fæces the ova exhibit no trace of segmentation or of differentiated embryo; but if placed in water, or kept moist and in a warm place, in the course of from five or six months—longer or shorter according to temperature—the embryo is developed,

and can be seen coiled up and moving about inside the egg-shell. If such an egg is accidentally or intentionally swallowed, on arrival in the stomach the shell is dissolved away and the contained embryo is set free. In a month it grows into a sexually mature animal, and, if both sexes are present, eggs in countless numbers are soon produced and appear in the fæces. Desiccation of the egg at atmospheric temperature does not destroy the embryo, which will quickly revive on becoming moistened. In many warm countries night-soil is the favourite fertiliser, and is regularly preserved and spread upon the fields. In this way the ova of ascaris obtain an opportunity of maturing, and in this way they have an opportunity of being swallowed by man. They may also be washed into drinking water; or, becoming desiccated on the drying up of the fields, be blown about as dust; or they may become attached to fruit or vegetables. In one of these, or in similar ways, they finally reach the human stomach and there attain maturity.

Symptoms.—In many instances the ascaris gives rise to no very noticeable symptom; in other instances it is to be credited with a number of ill-defined gastric and perhaps nervous troubles—capricious appetite, foul breath, restless sleep, peevishness, vague abdominal pains, nausea, and so forth. Sometimes the worms get into the stomach and are vomited, their appearance giving rise to no inconsiderable alarm. They may even creep up the œsophagus and into the mouth, or out by the nostrils. Cases are on record in which they caused suffocation by wandering, in this way, into the rima glottidis. They have also been known to enter the bile ducts and give rise to jaundice; to penetrate the intestinal wall and escape into the peritoneum, causing peritonitis; or to burrow into the abdominal walls and give rise to abscess. These accidents are fortunately of rare occurrence; their possibility, however, should be borne in mind and, apart from other obvious considerations, ought to

make us endeavour to rid patients of these troublesome guests as soon as possible. With this object in view, it was my practice in China to give my little patients, as a matter of routine, a few doses of santonin twice a year; very often the precaution received its justification by the appearance in the stools of one or more ascarides.

Adults, especially young adults, although to a much smaller degree than children, are liable to entertain these verminous visitors. Sometimes certain obscure dyspeptic symptoms in grown-up people will resist all treatment until three or four grains of santonin and a purgative have been administered. I had a patient once, who for a long time had been troubled with unaccountable nausea. One day, while he was sitting at breakfast, the feeling of sickness came on with unusual intensity. He had to leave the table and, after one or two retching efforts, brought up an ascaris lumbricoides. After this he was no more troubled with nausea. It is well, therefore, when puzzled over some obscure dyspeptic condition in tropical patients, to bear the ascaris in mind. If, for some reason, it is undesirable to give santonin unnecessarily, the stools ought first to be examined with the microscope. If ova (Fig. 70, *b*) are found, a dose or two of santonin may clear up diagnosis and cure the patient; if no ova are found, the drug may be withheld and the idea of ascarides abandoned.

Treatment.—The ascaris is readily expelled by a few grains of santonin. The dose is from half a grain to one grain for a child, three to four grains for an adult. A good plan of giving the drug is to prescribe three such doses on successive nights, the first and last dose to be followed by castor oil next morning. Patients, or mothers, ought to be warned about the peculiar effect santonin has on the urine and sometimes on the vision. I have only once seen any bad effects; in this instance a peculiar sort of intoxication, attended with delirium, which did not quite pass away for several days, followed its exhibition.

ANKYLOSTOMUM DUODENALE AND ANKYLOSTOMIASIS.

Ascaris lumbricoides, though an unpleasant parasite, cannot be considered a dangerous one, unless in very exceptional circumstances. It is otherwise with the ankylostomum (sometimes called dochmius duodenalis) which, in many countries, on account of the dangerous cachexia, called ankylostomiasis, it gives rise to, amounts to a positive curse.

Nomenclature.—The form of endemic anæmia with which this parasite is associated is of so marked a character that it has received a variety of distinctive names. Thus, in the French West Indies, severe ankylostomiasis is known as *cachexia aqueuse;* sometimes as *malcœur*, or as *mal d'estomac des negres;* in Colombia it is called *tuntun*, the sufferers being known as *tunientos;* in Brazil it has been called *oppilatio*, *opilaçao*, and *cançaço;* in Europe it is sometimes known as "miners' anæmia," or "tunnel disease," the latter in allusion to the notorious Saint Gothard epidemic; the form occurring in Egypt is spoken of as Egyptian chlorosis; in Ceylon it has been called beriberi; in Assam, according to Giles and others, it is the cause, or possibly a contributory cause, of the very fatal disease known as Kala-azar (p. 191); and, doubtless, elsewhere there are local names for this peculiar verminous anæmia.

Geographical distribution.—Since its discovery by Dubini in 1838, the ankylostomum has been found so widely diffused that it may be said to occur in all tropical and subtropical countries. Besides being abundantly present in the south of Europe, and in the tropical and subtropical regions of Asia and America, it has been ascertained to exist in North and South Queensland, Australia (*Trans. Intercolonial Med. Cong. of Australia*, 1893, Drs. Gibson and Turner), and in several of the islands of the Pacific. So prevalent is it in many parts of India that, according to Dobson (*Trans. First Ind. Med. Cong., Calcutta*, 1895), quite 75 per cent. of the inhabitants are affected. In Egypt it is found at

nearly every *post-mortem* examination; and there the anæmia it gives rise to is one of the most common causes for the rejection of recruits in the army. Thornhill (*Trans. First Ind. Med. Cong., Calcutta*, 1895) regards its ravages in Ceylon as far more serious than those of cholera; this, not on account of the number of deaths it causes directly, but on account of the vast numbers affected, the chronic nature of the disease, and the aggregate mortality, direct, and especially indirect, for which it is to be held responsible.

The parasite (Fig. 71).—The normal habitat of a. duodenale is the small intestine of man, particularly the jejunum, less so the duodenum, rarely the ileum or lower reaches of the alimentary canal; very occasionally it is found in the stomach. In these situations it attaches itself by means of its powerful buccal armature to the mucous membrane, from the blood of which it obtains a plentiful supply of nourishment. It is supposed to shift its hold from time to time, the abandoned bite continuing to ooze blood for a short period. It is said to be very prodigal of the blood it imbibes, the red corpuscles passing through its alimentary canal unchanged, the plasma alone being utilised.

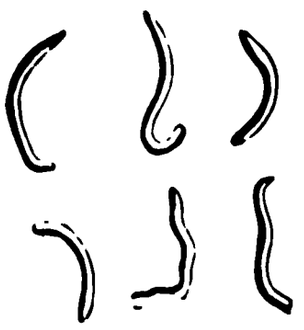

Fig. 71. — Ankylostomum duodenale, male and female. (*Blanchard.*)

The male and female ankylostomes — present generally in the proportion of one of the former to three of the latter—do not differ so much in size as is the case with many of the other nematodes. The male (Fig. 72) measures from 6 to 11 mm. in length by ·4 to ·5 mm. in breadth; the female 7 to 15 mm. in length by 1 mm. in breadth. Both sexes are cylindrical in form, white when they are alive, grey when dead, reddish-brown when full of blood. In both sexes the posterior end is the broadest part, whence the body tapers forwards to a narrow neck ending in a power-

fully armed, bulging and distinct mouth capsule. The margin of this remarkable organ is furnished with four strong, claw-like hooks—two on each side of the ventral line, and two conical teeth—one on each side of the dorsal line. The tail of the female is conical, and ends in a short delicate spine; the anus being subterminal, and the vagina opening on the ventral surface at the commencement of the posterior third of the body. The tail of the male is provided with a large umbrella-like, trilobate bursa possessing eleven ribs. Two long and very delicate spicules project from the cloaca which opens at the bottom of the bursa. Owing to the relative positions of the sexual openings the worms in conjugation look like the Greek γ.

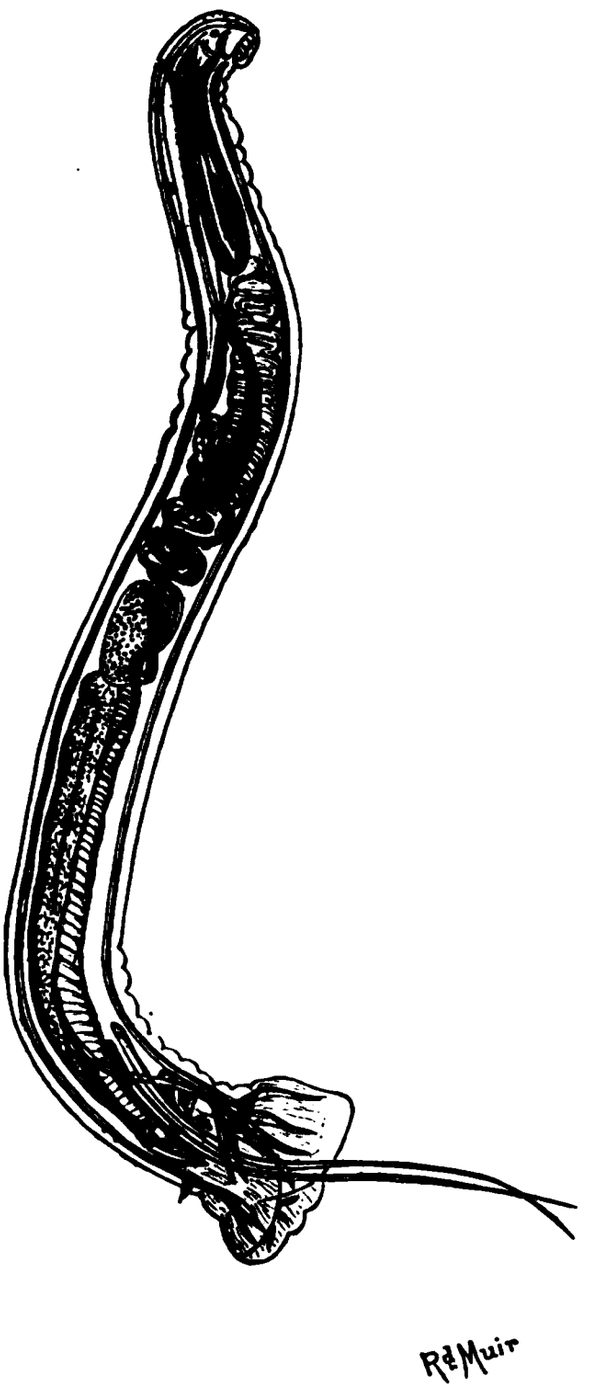

Fig. 72.—Male ankylostomum duodenale.

Reproduction and mode of infection.—The female ankylostomes produce a prodigious and never-ending stream of eggs (Fig. 70, *c*) which pass out in the fæces. As already stated, while in the body of the host the development of the embryo does not advance very far; but on leaving the human host it proceeds, in suitable circumstances, so rapidly that in one to two days a

rhabditiform embryo (·2 mm. by ·014 mm.) is born. This minute organism is very active, voraciously devouring what organic matter it can find and, for a week, growing rapidly (to ·56 mm. by ·024 mm.). During this time it moults twice. After the second moulting it passes into a sort of larval condition, in which it ceases to eat, and growth is suspended. In this state it may live for weeks or months, moving about more or less languidly in muddy water, in mud, or in damp earth. Should chance so determine, it is finally transferred to the human alimentary canal, either in muddy drinking water, or in the mud or dirt adhering to the hands or food dishes of the agriculturist, the brick-maker, or other operative engaged in handling the soil; or, it may be, in earth deliberately eaten by the geophagist. Arrived in its final host, after moulting again at the end of five weeks (Leichtenstern) it acquires sexual characters, and the permanent adult form. The duration of the life of a. duodenale in the intestine has not been determined; some state it in months, others in years (Sonsino)—one to three. On account of liability to reinfection, this point, an important one as affecting prognosis, is difficult to determine.

Giles (*Report on Kala-azar and Beriberi*, Shillong, 1890) holds that a. duodenale may become sexually mature while outside the human body and in the free state; in other words, that it is heterogenetic. His observations, so far as we are aware, have not been confirmed; though partially upheld by Sandwith, doubt has been thrown on their relevancy by Sonsino and Macdonald.

ANKYLOSTOMIASIS.

History.—Although Griesinger had previously shown that Egyptian chlorosis was due to the presence of the ankylostomum in the small intestine, and although similar observations had been made on negroes in America, it was not until the very fatal epidemic of anæmia among the miners in the

Saint Gothard tunnel (in 1880) had called the attention of European observers to the subject, that the real pathological importance of this parasite began to be properly apprehended. Multiplied observations have now shown that, although very minute, this blood-sucking parasite, if present in large numbers and for a length of time, more especially if its victims are poorly fed, is a very dangerous one indeed. The constant drain of blood it entails, the dyspepsia arising from the irritation caused by the wounds it inflicts on the mucous membrane, the consequent impairment of nutrition, and, possibly, as has been suggested, the absorption of some hæmolytic toxin—the product of the parasite—give rise to a grave cachexia, disqualifying to a greater or lesser extent the subject of it for work, and, not infrequently, leading to a fatal issue.

Its importance.—It must be borne in mind, however, that it is not in every instance in which the ankylostomum is present that consequences so serious ensue. There may be dozens of ankylostomes in the intestine without any appreciable anæmia, or, indeed, symptoms of any description whatever. Grave symptoms are the exception. One must be careful, therefore, to avoid concluding that the ankylostomum is the cause of every pathological condition with which it may chance to concur.

On the other hand, it must be borne in mind that many inhabitants of tropical and subtropical countries are in a state of chronic starvation. Living on coarse, bulky, innutritious food, they are prone to dilatation of the stomach and dyspeptic troubles. In such, any additional cause of malnutrition, as a swarm of ankylostomes, and a daily though perhaps small loss of blood, may be sufficient to turn the scale against them. In these countries, as elsewhere, there are many who live just on the borderland between health and disease; to such the ankylostomum may prove the last straw that breaks the camel's back.

It is evident that as a complication in typhoid, in

kidney disease, in dysentery, in malaria, in fact in any chronic or exhausting disease, the importance of this anæmia-producing parasite cannot be ignored.

The practitioner in the tropics, therefore, must be constantly on the outlook in all cases of anæmia, of dyspepsia, and of debilitated conditions generally, for the ankylostomum. He must bear in mind that this parasite, as will be presently pointed out, if permitted to remain in the intestine for a length of time, may be the cause, not only of anæmia, but of degenerations of various organs from which recovery is impossible. On this account, also, its early recognition becomes a matter of the first importance.

Further, ankylostomiasis is an important disease from the standpoint of the employer of native labour. The invaliding and inefficiency which it causes among coolies, not to mention the deaths, are often financially a serious matter to the planter and the mine owner. To them, any wisely directed expense or trouble undertaken for the treating and controlling of this helminthiasis, will be abundantly repaid by the increased efficiency of the labourer.

Symptoms.—The essential symptoms of ankylostomiasis are those of a progressive anæmia; an anæmia which is generally associated with dyspeptic trouble, but which, in uncomplicated cases, is not associated with wasting. If the progress of a case be unchecked, serous effusions in different organs and fatty degeneration of the heart ensue, and death may occur from syncope or from intercurrent complication.

One of the earliest symptoms of an extensive ankylostomum invasion is pain or uneasiness in the epigastrium. This is generally increased by pressure, but, for the time, may be relieved by food. The appetite, sometimes defective, is more often ravenous; but its gratification is apt to give rise to dyspeptic trouble of various kinds, to colic, to borborygmus, and, perhaps, to diarrhœa of imperfectly-digested food. Constipation may be present in some instances, irregularity of the bowels in others. The taste may

be perverted, some patients exhibiting and persistently gratifying an unnatural craving for such things as earth, mud, lime, what is called pica or geophagy. The stools sometimes, though rarely, have a reddish-brown tinge from admixture of half-digested blood. Sometimes they may contain small flakes of blood-tinged mucus. Pure blood is rarely passed. An extensive hæmorrhage, unless there be concurrent colitis, is still more rare, although *post mortem* considerable quantities of blood may be found in the small intestine. Fever of an irregular, intermitting, or even of a sub-continued type, is common. On the other hand, the temperature may be constantly sub-normal. Or these conditions may alternate. After a longer or shorter time, symptoms of profound anæmia gradually disclose themselves. The mucous surfaces and the skin become pallid, the face is puffy and the feet and ankles are swollen. All the subjective symptoms of a definite anæmia now become more and more apparent; there is lassitude, breathlessness, palpitations, tinnitus, vertigo, dimness of sight, mental apathy and depression, liability to syncope, and so forth. The circulation is irritable and hæmic bruits can be heard over the heart and larger blood-vessels. Ophthalmoscopic examination may reveal retinal hæmorrhages.

From some of these symptoms, were it not that with the advancing anæmia there is no loss of weight, one might be led to suspect the possibility of tuberculous or cancerous disease, Bright's disease, leucocythæmia, or an idiopathic pernicious anæmia. So far from losing weight, the patient may appear quite plump and, though hæmocytometric measurements testify to a slow and steady fall in the corpuscular richness of the blood until the lowest limit com patible with life is reached, there is no true poikilocytosis, no excessive leucocytosis, and not necessarily any enlargement of lymphatic glands, liver, or spleen. The hæmoglobin value of the corpuscles is not depressed correspondingly to the fall in their numbers.

The rate of progress is very different in different cases. In a few a high degree of anæmia may be attained, and even a fatal issue ensue, within a few weeks or months of the appearance of the first symptoms. Such rapid cases are rare; more frequently the disease is an exceedingly chronic one, ebbing, or flowing, or slowly progressing through a long series of years.

Should serious ankylostomiasis occur before puberty, the growth and development are apt to be delayed and stunted.

Diagnosis.—Provided its presence be suspected, ankylostomiasis is easily diagnosed. In tropical countries, anæmia without apparent cause should always suggest a microscopical examination of the fæces. If the ova (Fig. 70, *c*) of the ankylostomum duodenale are discovered, and no other reason for the anæmia be made out, the presumption is that the parasite is at the root of the mischief; at all events, no harm is likely to result from treatment based on this supposition. On the other hand, if no ova are found it must not be concluded that the case is not one of ankylostomiasis; for it sometimes happens that, in the later stages of the disease, symptoms will persist although the parasites which caused them in the first instance have disappeared, or have been got rid of by treatment. Permanent degenerations of the alimentary canal, of the heart, liver, kidneys, and blood-forming organs may remain, and even prove fatal, although the primary cause is no longer present. The history of the absence of other sources of anæmia is all we may have to go upon in such circumstances.

Ankylostomiasis is sometimes confounded with beriberi, and *vice versâ*. The presence of paralytic symptoms in beriberi, and their absence in ankylostomiasis, suffice for diagnosis. The anæmia of ankylostomiasis differs from that of malaria, inasmuch as the latter is accompanied by enlargement of the spleen, a sallow and perhaps pigmented

complexion, an icteric tint of the scleræ, occasional attacks of well marked periodic fever controlled by quinine, and, especially, the presence at such times of the plasmodium in the blood. Of course, ankylostomiasis and malarial cachexia may concur, and often do concur, in the same individual.

Some idea of the intensity of the affection may be got from an enumeration of the eggs in a given quantity of fæces; according to Grassi and Parona, 150 to 180 eggs per cubic centigramme indicate an infection of about a thousand worms, male and female.

Pathological anatomy and pathology.—As already mentioned, the bodies of the victims of ankylostomiasis are not wasted; on the contrary, there is plenty of fat in the usual situations. The appearance of plumpness is further increased by a greater or lesser amount of general œdema. There may be effusions in one or more of the serous cavities. All the organs are anæmic. The heart is dilated and flabby, its muscular tissue being in a state of pronounced fatty degeneration. The liver, also, is fatty and so are the kidneys.

If the *post-mortem* examination be made within an hour or two of death, the ankylostomes, in numbers ranging from a few dozens up to many hundreds, will be found still attached by their mouths to the mucous surfaces of the lower part of the duodenum, the jejunum and, perhaps, of the upper part of the ileum; but if the examination has been delayed for some hours, the parasites will have dropped their hold, and are then to be found lying in the mucus coating the inner surface of the bowel. Many minute extravasations of blood —some fresh, others of long standing—are seen in the mucous membrane, a minute wound in the centre of each extravasation representing the point at which the parasite had been attached. Sometimes blood-filled cavities, as large as filberts, are found in the mucosa; each cavity enclosing one or two worms and, probably, communicating by means of a small hole

with the interior of the intestine. Old extravasations are indicated by punctiform pigmentations. There may be evidence, in the shape of vesiculations and thickening of the mucosa, of a greater or lesser degree of catarrh. Occasionally, streaks or large clots of blood are found in the lumen of the bowel.

Daniels (*The British Guiana Medical Annual*, 7th issue, 1895) and others report that microscopic examinations of the liver and kidneys show the presence, within the cells of the parenchyma, of grains of yellow pigment having the reactions of hæmatoidin; indicating an intravascular blood destruction, such as occurs in pernicious anæmia and other diseases in which excessive hæmolysis is a feature. On this account, and also because he finds granules of a ferrous nature in the liver cells, Daniels concludes that the anæmia in ankylostomiasis is, in a measure, the result of blood destruction within the vessels by some toxic substance produced by the parasite and absorbed from the bowel. These results have not been confirmed by other observers; on the contrary, the late Dr. Beaven Rake (*Journal of Pathology*, Nov., 1894) concluded, from the results of a careful estimate of the amount of iron in the livers of five cases of ankylostomiasis, that in this disease the hepatic iron is below the normal average, and that the anæmia is entirely owing to the direct abstraction of blood by the parasites. The occurrence of the condition known as bothriocephalus anæmia lends a certain amount of probability to the toxin-hæmolysis theory. Further observations are necessary, however, before this question can be decided.

Treatment.—*Male fern.*—Until the introduction of thymol by Bozzolo in 1880, extract of male fern was the anthelmintic usually employed in ankylostomiasis. Male fern has still its advocates. It may be used where thymol fails—an occasional occurrence.

Thymol.—Before the administration of thymol the patient should be put on liquid diet for a day or two, and have the bowels well cleared out by an aperient.

In the morning, and following the action of the aperient, three or four ten- to thirty-grain doses of well triturated thymol, in cachets, in capsules, or in emulsion, are given on an empty stomach at intervals of an hour. If the bowels do not open spontaneously within four or five hours of the last dose another aperient dose should be given. Usually, by this treatment many ankylostomes are expelled and may be found in the motions. One such course of thymol may suffice; but it is well, after a week has elapsed, again to examine the stools microscopically, and, if it be found that ova are still being passed, to repeat the course of thymol once or oftener.

Certain precautions have to be observed in employing this drug. At times it gives rise to a very unpleasant form of intoxication—vertigo, excitement, etc., and the urine may become dark, as in carbolic acid poisoning. It is advisable therefore for the patient, while taking the drug, to keep his bed and to lie down for several hours after the last dose. Thymol is very insoluble in water, and is therefore, in ordinary circumstances, not readily absorbed in poisonous quantities; should, however, the patient, while thymol is present in the stomach, partake of any alcoholic drink, there is considerable risk of poisoning ensuing. Alcohol, ether, glycerine, turpentine, chloroform and oils are all solvents of thymol, and must therefore be avoided when this drug is being exhibited. Thornhill relates an instance in which a fatal result was brought about, apparently, by neglect of the obvious precautions suggested by these facts. A man had received thirty grains of thymol in water at 7 a.m. "He experienced no special symptoms after it, and at 9 a.m. the nurse gave him a second dose of thirty grains. As this man was supplied with arrack as an extra, and as in such cases a portion of the arrack was usually given at 9 a.m., the nurse gave it to him just after administering the second dose of thymol. The result was that intense collapse set in almost at once, and, notwithstanding all efforts, the man

coolies is to be recommended. At these inspections, all subjects of anæmia or dyspepsia should be put aside for more careful examination; if the ova of ankylostomes are found in their fæces a judicious dosing with thymol may avert serious disease in the individual, and also prevent him from becoming a source of danger to his companions.

In view of the great danger to health that exists in certain countries from this and similar parasites, the sanitary authorities in such places ought to circulate among the people, by means of printed leaflets or posters, a few simple directions for the prevention of ankylostomiasis and kindred diseases.

RHABDONEMA INTESTINALE AND RHABDONEMIASIS.

It sometimes happens while searching the fæces for the ova of the ankylostomum, that the observer is astonished by seeing a small, snake-like animal (Fig. 73, *a*) suddenly rush across the field of the microscope. On careful examination, this animal is found to be about 0·2 mm. or 0·3 mm. in length by 0·013 mm. in breadth; to have a sharply pointed tail and a rounded head; to be transparent; and to exhibit a short œsophagus which terminates in a double œsophageal bulb, the posterior end of which is provided with three tooth-like segments. This is, or rather was, called the anguillula stercoralis.

Anguillula stercoralis was discovered by Normand in 1876. For a time it was supposed to be a cause of a form of chronic diarrhœa very prevalent in Cochin-China. Later investigations, while clearing up the natural history of this parasite, have robbed it of any claim to pathological importance. It has been found that though the anguillula is not so common, its geographical distribution is about coextensive with that of the ankylostomum duodenale, and that the physical conditions demanded for the non-parasitic stages of these two worms are about the same. It has also been found that this so-called anguillula

stercoralis is the rhabditiform phase of the rhabdonema intestinale (Fig. 73, *b*) (formerly called anguillula intestinalis), a nematode which, in its parasitic form,

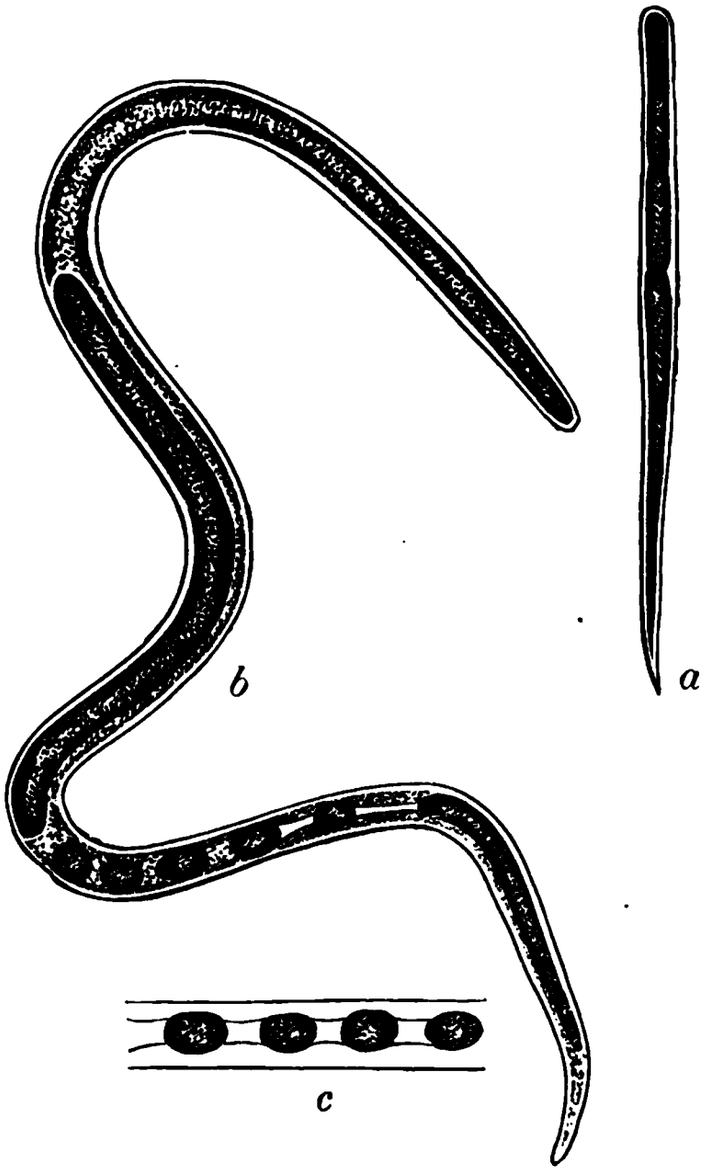

Fig. 73.—Rhabdonema intestinale.

lives in the mucus of the duodenum and upper part of the jejunum of man.

The rhabdonema is a very minute, slender worm, measuring 2 mm. in length by ·06 mm. in breadth. No male parasite has been discovered. The adult female is readily recognised by her minute dimensions, and by the string of five or six ellipsoidal eggs (·01 mm. by ·034 mm.) visible about the centre of the body.

On being passed into the contents of the bowel the ova develop with great rapidity; so that before leaving

the body of the host, unless during violent purgation, the embryo has escaped and is swimming about in the fæces, as already described, with great vigour, especially when these are fluid. Only in the event of violent purging do the ova appear in the stools; they may in this way be hurried out of the host before the embryo has escaped. Such ova are readily recognised by the way in which they are strung together, end on end, inside a delicate tube (Fig. 73, *c*). On leaving the body, unless they have access to some non-putrefying fluid, the embryos soon die; it is necessary, therefore, if we would follow their further development, to mix the fæces with water. If this mixture be kept at a low temperature the young rhabdonema develops into a filariform larva which, on being swallowed by man in drinking water, quickly assumes the mature parasitic form already alluded to. If, on the contrary, the cultivating medium be kept at a higher temperature, the embryos develop into male (·7 mm.) and female (1·0 mm.) rhabditic forms which, in time, produce in their turn filariform larvæ, similar to those obtained directly from the embryo in cold climates and capable, on being swallowed by man, of developing into mature rhabdonema intestinale.

The rhabdonema may produce some slight degree of catarrhal irritation of the bowel, though even this is doubtful. They have been found occasionally coiled up in the intestinal follicles, but no serious lesion can with certainty be attributed to their presence; a fortunate circumstance, as hitherto the use of anthelmintics has not proved effectual in procuring their expulsion. Sonsino recommends the prolonged exhibition of liquor ferri perchloridi in combination with small doses of thymol. It is probable that catarrhal conditions of the bowel favour these parasites, and that this is the reason for their being so frequently encountered in cases of chronic tropical intestinal flux. Treatment should therefore be directed to the cure of the catarrh.

The prophylaxis for rhabdonema is the same as that recommended for ankylostomum duodenale.

STRONGYLUS SUBTILIS.

Looss (*Centralblatt für Bakteriol.*, xviii., p. 161, 1895) has described a very delicate nematode frequently encountered in Egyptian fellahs. Its habitat is the upper part of the small intestine. The male, which is provided with two spicules, is from 4 to 5 mm. in length by 0·07 mm. in breadth; the female is slightly larger and is much more abundant than the male. The eggs are oval, thin-shelled, with an unsegmented vitellus, and measure 63 μ by 41 μ. This parasite does not occur in large numbers; and, as its mouth is unarmed and its dimensions exceedingly minute, it does not appear to give rise to any particular symptoms.

TREMATODES.

AMPHISTOMUM HOMINIS (FIG. 74).

This minute trematode, discovered in the cæcum and colon of two Indians in Calcutta by Lewis and MacConnell in 1876, measures 5 to 8 mm. in length by 3 to 4 mm. in breadth. It is readily recognised by its large posterior sucker, which is terminal and greatly exceeds in breadth the rest of the body. It attaches itself to the mucous membrane of the bowel by means of this sucker. The ova, which are operculated at the smaller end, average 150 μ in length by 72 μ in breadth. Nothing is known of the life-history.

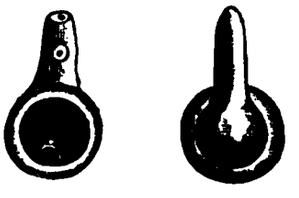

Fig. 74.—Amphistomum hominis. (Nat. size.)

This trematode has been found by Giles in natives of Assam, and by Law in an East Indian immigrant in British Guiana.

Distomum Buski (v. crassum) (fig. 75).

Distomum Buski, over an inch in length, is the largest of the distomes inhabiting man. It has been found in China, Sumatra, the Straits Settlements, Assam, and in India, and by Law in an East Indian immigrant in British Guiana. It is an elongated oval in shape, rather narrower anteriorly than posteriorly, fleshy, and covered with minute spines. The suckers are placed close together. The ova are oval, 125 μ by 75 μ, and are closed, I find, by a very delicate operculum. In two recorded instances (Cobbold) d. Buski was associated with attacks of recurring diarrhœa and other signs of intestinal irritation. It probably inhabits the upper part of the small intestine. Nothing is known of the life history. It may be expelled by thymol given as for ankylostomum.

Fig. 75. Distomum Buski (Nat. size.)

Distomum heterophyes (fig. 76).

Distomum heterophyes is the smallest distome, so far as known, inhabiting man. It measures 1 to 1½ mm. in length by 0·7 mm. in breadth. It is of a bright red colour. The anterior, narrower, and more mobile part of its body is covered with minute spines. The eggs are reddish brown, and measure 26 μ by 15 μ. It was discovered by Bilharz in 1851, in Cairo, in the small intestine of a child, the little parasites looking like red points on the mucous surface. Since that time it has

Fig. 76. Distomum heterophyes. (Magnified.)

been found in Egyptians by other observers. Nothing is known of its life-history. It is believed to be innocuous.

CESTODES.

The ordinary tape-worms, tænia saginata and tænia solium, and their respective cystic forms, are common enough in the tropics and sub-tropics, their distribution being regulated by the presence or absence of their proper intermediate hosts—the ox in the one case, the pig in the other—and by the habits of the people as regards cooking and conservancy. Tænia echinococcus of the dog, and its cystic form—hydatids—are found wherever the dog and sheep are found—that is, practically, everywhere. Bothriocephalus latus is known to occur in Turkestan, in Japan, where the natives are in the habit of eating raw fish, and among the natives on the shores of Lake 'Ngami, South Africa. Ichthyophagous habits are probably responsible for the occurrence of the large tape-worm described by Blanchard under the name Krabbea grandis, which Ijima and Kurimoto found in a Japanese from the province of Hizen (*Comptes rendus de la Soc. de Biologie*, I., p. 609, I., 94).

The only cestodes of man which, so far as known, have any claim to be regarded as more or less special to warm climates are tænia nana, tænia Madagascariensis, and bothriocephalus Mansoni. Doubtless there are other species which, so far, have escaped observation.

TÆNIA NANA (FIG. 77).

This minutest of the tape-worms inhabiting man was first found as a human parasite by Bilharz, in Cairo, in 1852. In recent years it has been identified with tænia murina of the rat and other rodents. It has a somewhat extensive geographical distribution. In the case of man, at all events, it seems to have a predilection for warm countries. Besides Egypt, it

has been found in Italy, Buenos Ayres, and in Bangkok, Siam. It is readily recognised by its small size 10 to 15 mm. in length with a maximum breadth of 00·7 mm. It has from 150 to 200 joints, the head being furnished with a retractile proboscis surrounded by a single row of from twenty-four to twenty-eight hooklets. The ova are oval or round, 30 to 37 μ in diameter, they are possessed of three membranes, within which the hexacanth embryo can with difficulty be made out. Grassi has shown that, in the rat, the embryo of this cestode penetrates the mucous membrane of the intestine, and there develops into its cysticercus. After a time this cysticercus ruptures, permitting the head to escape and attach itself to the mucous membrane, where it speedily grows into the mature tape-worm.

Fig. 77 Tænia nana (Magnified.)

Cases are on record in which the human intestine was beset with hundreds of these minute parasites which, by their presence, gave rise to marked symptoms of gastro-intestinal irritation. They are readily expelled by male fern.

TÆNIA MADAGASCARIENSIS.

Discovered by Grenet in Mayotte (Madagascar), this parasite has since been found in Mauritius, in Bangkok, and by Dr. Daniels (*Lancet*, Vol. ii, p. 1,455, 1896) in a Demerara Indian. On account of its wide geographical range, Blanchard (*Bul. de l'Acad de Med*, Jan. 12th, 1897) remarks that its intermediate host is probably some insect of similar distribution, possibly, he suggests, one intimately associated with ships—the cockroach (periplaneta orientalis), for example.

Tænia Madagascariensis attains a length of from 25 to 30 cm., and is made up of from 500 to 600 trapezoid joints. The head terminates in a massive rostellum surrounded by a double circle of ninety hooklets 18 μ in length. The suckers are round and of considerable size. The genital pore is unilateral. In the ripe segments the ova are agglomerated into a number of separate rounded masses.

So far as known, the symptoms produced by this parasite correspond with those caused by the more familiar tape-worms. It is probably amenable to filix mas.

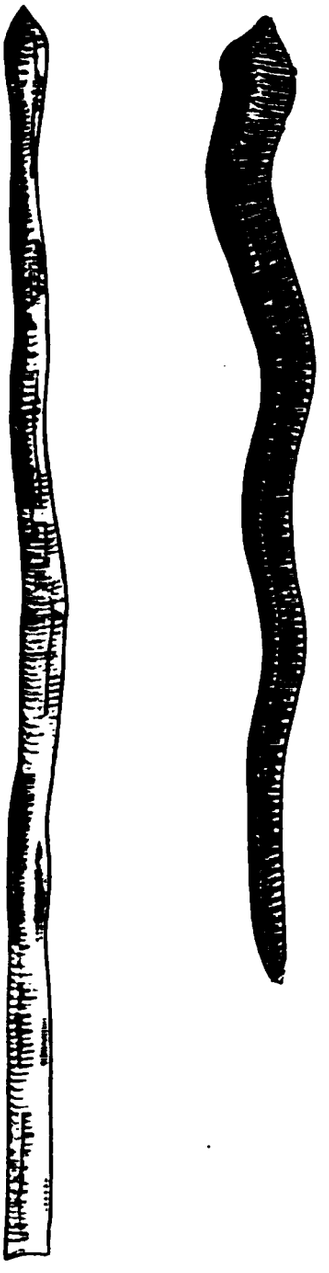

Fig. 78.—Bothriocephalus Mansoni. (*From specimens preserved in spirits and therefore shrunken.*)

BOTHRIOCEPHALUS MANSONI (Fig. 78.)

This parasite, the larval form of an unknown species of bothriocephalus, was discovered by the writer in making the *post-mortem* examination of a Chinese in Amoy. A number of specimens were found lying under the peritoneum in the neighbourhood of the kidneys and iliac fossæ, and also one, apparently a free specimen, in the pleural cavity. They were more or less coiled up and irregularly disposed in the subperitoneal fascia, looking like ribbon strings of fat until they were turned out when they exhibited feeble yet distinct movements. No differentiated head, no definite structure, and no evidence of sexual organs could be discovered; neither was there any attempt at segmentation visible. When fresh, the parasites measured about 30 to 35 cm. in length by about 2·5 mm. in breadth. They were flat and tapered slightly

towards one end. At the broader end there was a sort of papilla which, in some instances, was retracted. Scheube extracted a similar parasite from the urethra of a Japanese; it has also been found in Bathurst, Australia. Daniels has quite recently found this or a similar parasite in a Carib in British Guiana.

Leuckart suggests that the definitive host of this parasite is probably a carnivorous animal closely associated with man.

LARVÆ OF DIPTEROUS INSECTS.

A residence in the alimentary canal of some vertebrate animal is a regular feature in the life-history of many dipterous insects. The ova of the insect are either licked from the skin, or swallowed in the food on which they had been deposited. In this way they get transferred to the stomach where, after a time, the larva is hatched out and proceeds in development. In due course it appears in the fæces. Man is not infrequently victimised in this way, especially in tropical countries. Sometimes, until a correct diagnosis is arrived at, not a little alarm is caused by the appearance of these creatures in the stools. They are easily recognised. The ringed, cylindrical body, from ¼ inch to 1 inch in length according to species, broad at one end, tapering at the other, and usually beset with little spines or hairs, is sufficiently diagnostic (Fig. 79). A dose of castor oil will probably expel any that may not have been passed spontaneously.

Fig. 79. Larva of [illegible] vomitoria (the blue bottle fly). (Upper figure magnified.) (*Leuckart.*)

SECTION VI.—SKIN DISEASES.

CHAPTER XXXVII.

DISEASES OF THE SKIN.

I.—*Non-specific.*

PRICKLY HEAT.

PRICKLY heat or, as it is sometimes called, lichen tropicus, is a form of miliaria (not of lichen) connected with the excessive sweating incident to the heat of tropical climates. Nearly every European in the tropics suffers from it, particularly during the earlier years of residence. Some never seem to become acclimatised in this respect, but continue year after year to exhibit their crop of prickly heat when the hot season comes round.

Though sufficiently annoying in the robust and healthy, in them prickly heat is not a grave affair. It is otherwise in the case of the invalid, of delicate sickly children, of hysterical and, especially, of parturient women; to these it may prove, by interfering with sleep and provoking restlessness, a very serious matter. Prickly heat is also a common though indirect cause of boils; for the breaches of surface, following on the scratching it induces, afford many opportunities for the invasion of the micro-organisms of that disease.

Prickly heat consists of a miliary eruption, generally most profuse on those parts of the body, as around the waist, which are closely covered with clothing; but it also occurs on the backs of the hands, on the forehead, occasionally on the face, the scalp, in fact on any part of the surface of the body. The minute, shining, glass-like vesicles, and the numerous, closely set, and slightly inflamed papules give the skin the feeling as if thickly sprinkled with grains of

sand. The eruption may keep out for months on end, becoming better or worse according to circumstances. The pricking and itching are often exceedingly distressing. Anything leading to perspiration immediately provokes an outburst of this almost intolerable itching—nothing more certainly than a cup of hot tea or a plate of hot soup. Long drinks, exposure to the hot sun, close rooms, warm clothing, all aggravate the distress. Sometimes the little vesicles may pustulate, doubtless from micrococcus infection. So soon as the weather becomes cool the irritation and the eruption quickly subside.

Treatment.—Manifestly the most important thing is the avoidance of all causes of perspiration—particularly the copious consumption of fluids, especially hot fluids, moderation in exercise, avoiding close rooms, warm clothing, and so forth. The sleeping mattress and pillow should be covered with a finely woven grass mat, and the bed provided with what is known in the East as a "Dutch wife"—that is a hollow cylinder, 4 feet by 8 or 10 inches, of open rattan work, over which the arms and legs can be thrown and unnecessary apposition of sweating surfaces so avoided. A pankah at night is a great comfort. Many things have been recommended as preventives; for example, rubbing the body over after the bath with the juice of a lemon, Jeyes' fluid or bran in the bath, etc. Every bath-room in the tropics should be provided with some mildly astringent and antiseptic dusting powder. A very good one consists of equal parts of boric acid, oxide of zinc and starch. This should be freely applied after careful drying of the skin, particularly to the axillæ, crutch, under the mammæ in women, and between the folds of skin in fat children and adults. A simple precaution of this sort saves much suffering both from prickly heat and epiphytic skin disease. Sometimes the following powder, gently rubbed in for five or ten minutes with a damp sponge, cures bad patches of prickly heat:—Sublimed sulphur, 80 parts; magnesia,

15 parts; oxide of zinc, 5 parts. Lotions of calamine, with or without hydrocyanic acid, or of carbolic acid, relieve the itching temporarily.

II.—*Caused by bacteria.*

TROPICAL SLOUGHING PHAGEDÆNA.

Definition.—A rapidly spreading, but generally after a time spontaneously arrested, gangrene of the skin and subjacent tissues, resulting in the formation of a large sloughing sore. Though occasionally fatal, these sores, as a rule, under favourable conditions, granulate and cicatrise, or become chronic ulcers.

Geographical distribution. — Sloughing phagedæna is common in most tropical countries, particularly in those with a hot, damp climate. These sores are often named after those districts in which they are specially prevalent; thus we hear of Mozambique ulcer, Yemen ulcer, etc. They are found principally in jungle lands, less frequently in towns and well settled districts. Whether tropical sloughing phagedæna and the hospital gangrene at one time so prevalent in the hospitals of Europe, are the same disease it is difficult to say. They agree in some respects; but in the marked tendency of the tropical sore to self-limitation, and, possibly, as Scheube points out, in its feebly infective power there is some indication of a specific difference.

Ætiology.—Doubtless depending on the proliferation in the affected tissues of some specific micro-organism, not yet satisfactorily separated, the germ of sloughing phagedæna finds its special opportunity in the bodies of men who, from overwork, underfeeding, exposure, malaria, dysentery, scorbutus, and the like, are physically depressed. Thus it is apt to attack the half-starved, malaria-stricken pioneers in jungle lands, overdriven slave gangs, and soldiers campaigning in the tropics. In such circumstances a slight wound, an abrasion, even an insect bite, or an old chronic ulcer may serve

as the starting-point for one of these terrible sores. Where yaws and sloughing phagedæna are co-endemic, the sores of the former may become infected with the virus of the latter, and serious sloughing and cicatricial contractions result. The feet and legs, being most exposed to injury, are the most frequent locations for this form of ulceration, but the arms or any other part of the body may also become infected.

Symptoms.—If the disease occur in previously sound skin the first indication is the formation of a large bleb with sero-sanguinolent contents. Its formation may be attended with some pain and constitutional irritation. When, in the course of a few hours, the bulla ruptures, an ash-grey, moist slough is exposed. The sloughing process rapidly extends in all directions until the skin and subcutaneous fascia, over an area many inches in diameter, are converted into a yellowish, moist, horribly stinking slough. After a few days the centre of the slough begins to liquefy, the sore still continuing to extend at the periphery. In the course of a week or longer the sloughing process may cease and the slough be gradually thrown off. Then it is seen that not only have the skin and superficial fascia been destroyed, but that possibly muscles, tendons, nerves, vessels, and even the periosteum of the bones have shared in the gangrenous process. Fortunately in many instances the deeper structures are spared, the disease being relatively superficial. Sometimes, however, important structures including joints, bones and large blood-vessels, are destroyed; in such cases, even if life be spared, great deformity may ensue from different forms of ankylosis, or from strangulation of a distal part by a contracting cicatrix.

When the disease attacks a pre-existing wound or sore, the granulating surface of this becomes dry, and rapidly assumes the appearance and characters of a slough.

In sloughing phagedæna the neighbourhood of the sore is somewhat congested and swollen, particularly

so if the patient has been obliged to use the limb. Constitutional disturbance may be considerable and of an adynamic type. On the other hand it occasionally happens that large sores are attended with singularly slight local or general reaction. In bad cases a sapræmic condition is apt to supervene and carry off the patient; or death may occur from bleeding from the opening of a large blood-vessel.

Treatment.—It is of the first importance to endeavour to correct any cachectic state which may be present. Thus good food, fresh vegetables, lime juice, and quinine are almost invariably indicated. Opium in full doses, not merely to assuage pain, but on account of its special action on the phagedænic process, is usually of great service. Locally, an endeavour must be made effectually to destroy the diseased surface by some powerful and penetrating caustic. With this view, I recommend that the patient be put under chloroform, and the slough thoroughly dissolved off by the free application of pure carbolic acid, a piece of lint on a stout stick being used as a mop for the purpose. Thereafter the limb should be elevated and placed under some improvised irrigator from which a weak, warm antiseptic solution should continuously trickle over the now clean surface. If the phagedænic action recur the carbolic acid must be promptly reapplied as often as may be necessary. On healthy granulations springing up the ulcer is to be treated on ordinary principles.

BOILS.

The anatomical and clinical features of this painful affection are too familiar to require detailed description. Suffice it to say that a boil is produced by the proliferation of certain micro-organisms—torula pyogenica or others—in the skin and subcutaneous tissue; that the organism gives rise to local and limited infiltration of the tissues with lymph which subsequently and rapidly necroses, the necrotic core being surrounded by an areola of acute inflammation;

that this core is separated by a process of sloughing and so got rid of, the resulting ulcer speedily healing and leaving a depressed scar which, when occurring about the legs, may become pigmented. Though a self limiting disease locally, it is nevertheless capable of being inoculated elsewhere in the same individual, both through a breach of surface and, also, by simple contact of the discharges with the skin, the micro-organism apparently entering by a hair follicle. This inoculability of boils is apt to be overlooked.

Conditions of debility, presumably by lowering resistance, predispose to boils, the subjects of diabetes are specially prone to them, the saccharine state of the blood or secretions seeming to be particularly favourable to growth of the specific germ.

At one time or another few Europeans in the tropics escape an attack of boils. In some instances crop after crop succeeds one another, the individual boils being so numerous that the patient is quite unfitted for work by the attendant pain and fever. In certain years so many members of a community are attacked that the disease may be described as being epidemic. These epidemics, occurring when some particular fruit is in season, are very generally, but probably incorrectly, attributed to the use of the particular fruit in question Mangos are frequently held responsible; probably in error.

Treatment. Any constitutional irregularity must be treated appropriately. Malaria demands quinine; anæmia and debility, iron and wine; constipation, aperients; diabetes, a suitable diet. I have never seen any good from such vaunted specifics as calcium sulphuret, tar water, or yeast.

Boils ought never, unless in very exceptional circumstances, to be poulticed. Poulticing, although it may relieve the pain of the existing boil, is prone to be followed by more boils in the area sodden by the heat and moisture. Neither should boils be incised or squeezed. The only exceptions to the rule for not cutting is in the case of boils occurring in

the scalp or axilla. In the former situation, unless opened early, they are apt, especially in young children, to burrow and cause troublesome abscesses; in the latter situation boils tend to be very indolent and painful, and do not readily spontaneously break through the lax integuments.

In any situation in which the boil is liable to be irritated by pressure or clothing, it is sometimes a good plan to cover the part with a circle of wash leather spread with soap plaster, and having a small hole cut in its centre corresponding to the centre of the boil. When a boil opens, the discharge must be kept from soiling the adjoining skin, and the patient must be warned against touching the skin elsewhere with soiled fingers. The parts must be frequently cleansed with 1 in 1,000 corrosive sublimate lotion, powdered with boracic acid and starch, and covered with a clean dry antiseptic dressing. A threatening boil may often be aborted by touching the little initial itching or vesiculated papule with some penetrating antiseptic, as iodine tincture, or by painting it with collodion. A very successful method is to drill slowly into the centre of the papule with a pointed pencil of hard wood dipped in pure carbolic acid. The point of the pencil should penetrate at least an eighth of an inch, and should be frequently recharged with the acid during the drilling process; the pain is trifling. In this way, in a severe attack of furunculosis, boil after boil may be aborted and the attack brought to an end.

Change of air is necessary at times in severe cases.

PEMPHIGUS CONTAGIOSUS.

Definition.—A non-febrile, highly contagious skin disease peculiar to warm countries. It is characterised by the formation of large vesicles or bullæ which are unattended by marked inflammation, ulceration, or the formation of crusts or scars.

Geographical distribution. Pemphigus contagiosus is very common in south China during the

hot weather; in some years it may be described as being epidemic. It is perennial in the Straits Settlements, and it is known in Madras. Doubtless, although it has escaped notice by most medical writers, it is common enough elsewhere in the tropics, or wherever heat and moisture combine to bring about a state of skin favouring its development on the infective material being supplied. It is especially common in schools and similar institutions where large numbers of children are thrown much together; they readily pass the disease one to the other. European children are more prone to it than native children; European adults are by no means exempt, but the native adult is rarely affected.

Symptoms.—Pemphigus contagiosus closely resembles certain forms of the impetigo contagiosa of temperate countries, and is doubtless a variety of this class of skin disease. The individual lesions, as can readily be ascertained by inoculation experiments, begin as minute erythematous specks which rapidly proceed to the formation of vesicles, bullæ, or even large pemphigus-like blebs. The little blister springs abruptly from sound skin; there is no areola of congestion. For a short time the hemispherical bleb is beautifully pellucid, tense, and shining. Presently, however, the serous contents become somewhat turbid, and the blister gets flaccid and dull. At this stage, either from scratching or pressure, the blister is generally ruptured. The morbid process does not come to an end, however, but proceeds as an advancing, eccentrically-spreading exfoliation of the epidermis; an exfoliation which may not cease to advance until an area an inch or more in diameter is denuded of epithelium. Then, in that particular spot, the disease stops, a pinkish, slightly glazed looking patch, rarely covered with a tissue paper-like scale, remaining for some time. Occasionally, after the rupture of the primary bleb, vesication may continue in the peripheral portion of its remains. Only one or two spots may be visible on the entire surface of

the body; generally there are many, the disease being spread by the fingers in scratching or rubbing.

Pemphigus contagiosus may occur in almost any part of the body. In young children it is usually diffuse; in adults it is mostly confined to the axillæ and crutch. In these latter situations it gives rise to much irritation and discomfort, owing to the successive crops of bullæ running into each other and rendering the parts raw and tender, and predisposed to boils or some form of eczematous intertrigo. During warm, moist weather it may be kept up indefinitely by auto-inoculation.

Assistant-Surgeon Soorjee Narain Singh describes (*Trans. First Ind. Med. Cong.*, 1895) a series of cases of a form of contagious pemphigus occurring in rapid succession in the children of three families in India (exact locality not specified), which bears some resemblance to the pemphigus contagiosus above described. It differs, however, inasmuch as in the Indian disease the bullæ were very large—often larger than hen's eggs, and persisted for from one to three weeks. In one of the thirteen cases described there followed a certain amount of sloughing at the seat of the bullæ; in the others there was neither ulceration nor constitutional disturbance.

Ætiology and pathology.—Like ordinary impetigo contagiosa, this is undoubtedly a germ disease. I have found a diplococcus in the epidermis and fluid of the blister; whether this is the special bacterium responsible for the disease, cultivation and inoculation experiment have not yet decided.

Diagnosis.—Absence of constitutional symptoms, or a history of such, distinguishes pemphigus contagiosus from chicken-pox. Absence of trichophyton elements and of a well-defined, slightly raised, festooned, and itching margin, together with the presence of large blebs and scaling of the epidermis, distinguishes it from ordinary forms of body ringworm; a disease with which, when occurring in the armpits and crutch in adults, it is often confounded.

Treatment.—Cleanliness, the frequent use of a bichloride of mercury lotion (1 to 1,000), and a dusting powder of equal parts of boracic acid, starch, and zinc oxide are speedily effective. In the school and nursery those responsible for the care of children must be informed of the contagiousness of this unpleasant affection, and measures be instituted accordingly.

III. *Caused by vegetable parasites.*

MYCETOMA, OR THE FUNGUS FOOT OF INDIA.

Definition. A disease of warm climates, particularly of India, affecting principally the foot, occasionally the hand, rarely other parts of the body, never the internal organs. It is characterised by enlargement and deformity of the part; an oily degeneration and general fusion of the affected tissues, the formation of cyst-like cavities communicating by sinuses, and containing peculiar mycotic aggregations in an oily purulent fluid which escapes from fistulous openings on the surface. The disease runs a slow course, is never recovered from spontaneously, and, unless removed, terminates after many years in death from exhaustion.

History and geographical distribution. The earliest notice of this disease we owe to Kæmpfer (1712). Its more modern history commenced with Godfrey, of Madras, who, in the *Lancet* of June 10th, 1843, gave a description of several unquestionable examples under the title, "Tubercular Disease of the Foot." Subsequently Balingall (1855), who was the first to suggest its parasitic nature, Eyre (1860), and others added considerably to our knowledge of the subject. The merit of bringing the disease prominently before the profession, and of distinctly describing its clinical and anatomical features, as well as of suggesting its probable pathology, belongs entirely to Vandyke Carter who, from 1860 to 1874, in a series of important papers, furnished the information on

which all later descriptions have been principally founded. Carter was the first to point out the presence of mycotic materials in the discharges coming from the implicated structures, and in the contents of the characteristic cysts and sinuses with which they are honeycombed. Since the date of Carter's papers, beyond the discovery that the associated fungus, in at least one variety of mycetoma, possesses affinities to actinomyces, as suggested by him in 1886, and that the disease is not confined to India, there has been no very important addition to our knowledge.

In India mycetoma is endemic in districts more or less limited. These districts are scattered over a wide area, the intervening regions—in some instances whole provinces, as that of Lower Bengal—enjoying an almost complete immunity. It appears to be acquired only in rural districts, the inhabitants of the towns being exempt. Among the most afflicted districts may be mentioned Madura—hence the name "Madura foot" by which mycetoma is often known—Hirsar, Ajmeer, Delhi, various places in the Punjab, Kashmir, and Rajputana. In recent years we have accounts of its occurrence with some degree of frequency in Senegambia, and, also, of a very few examples in Algeria, in Cochin-China, in Italy, and, possibly, in the United States and in South America. It is probable, therefore, that in time mycetoma will be found to be endemic in many warm countries in which it is at present unrecognised.

Symptoms.—Mycetoma begins usually, though by no means invariably, on the sole of the foot—most often the right. The first indication of disease is the slow formation of a small, firm, rounded, somewhat hemispherical, slightly discoloured, painless swelling perhaps about half an inch in diameter. After a month or more this swelling may soften and rupture, discharging a peculiar viscid, syrupy, oily, slightly purulent, sometimes blood-streaked fluid, containing in suspension certain minute, rounded, greyish or

yellowish particles, often compared to grains of fish roe. In other examples of the disease the particles in the discharge are black, having the size and appearance of grains of coarse gunpowder. Sometimes these particles are aggregated into larger masses up to the size of a pea. In time additional swellings, some of which break down and form similar sinuses, appear in the neighbourhood of the first or elsewhere

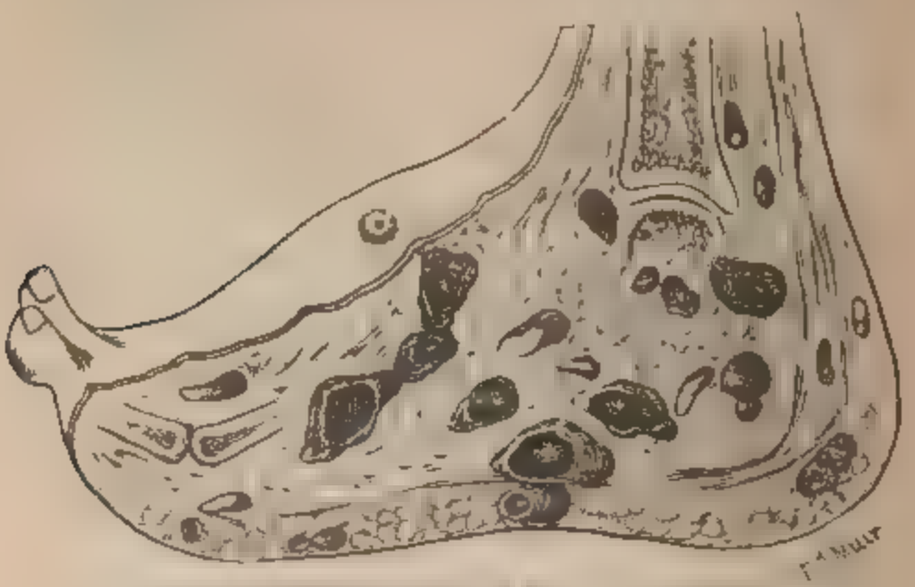

Fig. 80. Mycetoma, or "Madura foot." (*T. R. Lewis.*)

about the foot. For the most part the sinuses are permanent, healing up in a very few instances only. Gradually the bulk of the foot increases to perhaps two or three times the normal volume (Fig. 80). There is comparatively little lengthening of the foot; but there is a general increase in thickness, so that in time the mass comes to assume an ovoid form, the sole of the member becoming convex, the sides rounded, and the anatomical points obliterated. The toes may be forced apart, bent upwards at the tarso-phalangeal joints or otherwise misdirected, so that, on the foot being placed on the ground, the toes do not touch it. The surface of the skin is roughened by a number of larger or smaller, firmer or softer, hemispherical

elevations, in some of which the orifices of the numerous sinuses open. Most of these orifices are easily made out; others are not so apparent, their position being indicated and, at the same time, concealed by a bunch of pale, flabby, fungating, and but slightly vascular granulations. In the latter the orifice may be hard to find; once the probe is got to enter, however, the instrument readily passes to a considerable depth, even to the bone. In advanced cases it can be carried through the softened tissues with the greatest ease in almost any direction, and without causing much pain or hæmorrhage.

The discharge issuing from the sinuses differs in amount in different cases, and from time to time in the same case; whether profuse or scanty it always exhibits the same oily, mucoid-like, slightly purulent appearance, and may stink abominably. With a very few exceptions it contains either the grey or the black grains already referred to, rarely similar bodies of a reddish or pink colour.

To the touch the swollen foot feels somewhat elastic, and does not readily pit on pressure. The sensibility of the skin is preserved. Although complained of in some instances, severe pain is rarely a prominent feature. The principal complaint is of inconvenience from the bulk and weight of the mass, and, in advanced cases, of the uselessness of the limb for locomotion. In time the foot is no longer put to the ground, different unnatural styles of progression being adopted by different patients.

As the foot enlarges the leg atrophies from disuse; so that in the advanced disease an enormously enlarged and misshapen foot, flexed or extended, is attached to an attenuated leg consisting of little more than skin and bone. In some the tibia, or the bones of the forearm, as the case may be, become involved; in others the disease may be at first confined to a toe, or a finger, or other limited area. In a very few instances the seat of the disease is the knee, thigh, jaw, or neck. The internal organs are never implicated,

either primarily or secondarily; neither are the lymphatic glands, although these may be the subject of adenitis from septic infection.

After ten or twenty years the patient dies, worn out by the continued drain, or carried off by diarrhœa or other intercurrent disease.

Classification.—Although the broad clinical features, and the progress of all cases of mycetoma are practically identical, it is customary to divide them into three varieties according to the colour of the particles suspended in the discharge which particles, as will be presently explained, proceed from larger masses of the same coloured material lodged in the diseased tissues. Thus we have the white or ochroid, the black or melanoid, and the red forms of mycetoma. The first is the most common form, the second is somewhat less common, the third is very rare.

Morbid Anatomy.—On cutting into a mycetomatous foot or hand the knife passes readily through the mass, exposing a section with an oily, greasy surface, in which the anatomical elements in many places are unrecognisable, being, as it were, fused together, forming a pale, greyish-yellow mass. The bones in many places have entirely disappeared, where their remains can still be made out the cancellated structure is very friable, thinned, opened out, and infiltrated with oleaginous material. Of all the structures the tendons and fasciæ seem to be the most resistant.

The most remarkable feature revealed by section is a network of sinuses and communicating cyst-like cavities of various dimensions, from a mere speck to a cavity an inch or more in diameter. Sinuses and cysts are occupied by a material unlike anything else in human morbid anatomy. In the black variety of mycetoma this material consists of a black or dark brown, firm, friable substance which, in many places, stuffs the sinuses and cysts; manifestly it is from this that the black particles in the discharge are derived. In the white variety

the sinuses and cysts are also more or less stuffed by a white or yellowish roe-like substance, evidently an aggregation of particles identical with those escaping in the corresponding discharge. The black substance which can be readily turned out, is moulded into truffle-like masses ranging in size from a mere grain to a small apple, according to the capacity of the cyst or sinus containing it. The roe-like particles in the white variety are held together by a softer cheesy-looking material. The sinuses and cysts occupy the bones, muscles, or fasciæ indiscriminately; they are found principally in the fat and connective tissue. They are lined by a smooth membrane, adherent where in the soft tissues, but capable of being enucleated where in the bones. Some of the cysts do not communicate with sinuses; most of them, however, do so and with each other, opening on the surface of the skin at the mammillated fistulæ already referred to. In the very rare red variety the colour of the accretions is red or pink. In a few instances—as in those recorded by Lewis and Cunningham—no concretions of any description can be discovered, the cysts and sinuses being occupied by an oleaginous purulent material alone.

Under the microscope mycotic elements can be discovered both in the white and black concretions. In microscopical sections of the tissues evidences of extensive degenerative changes, the result of a chronic inflammation, can be readily made out. An important feature as bearing on the pathology of the disease, and one which was long ago described by Lewis and Cunningham, has been insisted on by Cunningham (*Scient. Mem. by the Med. Off. of the Army of India*, part 9, 1895), namely, a sort of arteritis obliterans or extensive proliferation of the endothelium of the arteries and, according to Vincent (*Ann. de l'Instit. Pasteur*, 1895), a thickening of the adventitia of the vessels as well as of the capillaries in the more affected areas.

Histology, pathology, and ætiology.—*White*

variety.—The white particles suspended in the discharge from the white or ochroid variety of mycetoma are soft, easily crushed, insoluble in caustic potash, alcohol, chloroform, or acids. They are round or somewhat reniform in shape and, under the microscope, are seen to be made up of an agglomeration of several colonies of a ray fungus—closely resembling actinomyces—in the meshes of which cellular products of inflammation are entangled.

As in actinomyces there is a central reticulum of an exceedingly fine and interwoven mycelium surrounded by a closely set radiation of delicate, straight filaments (1 μ to 1·5 μ) many of which terminate in well-marked club-shaped ends. These clubs thus constitute the peripheral layer in a three-zoned body, the middle zone being the straight filaments, the central zone the interwoven mycelium. The roe-like masses in the cysts and sinuses are but aggregations of the rounded fungus group constituting the individual granule.

Sections show the same parasite in the diseased and softened tissues outside the cysts and tunnels. Thus Vincent (*Ann. de l'Inst. Pasteur*, No. 8, 1894) found it in the unbroken tuberose swellings under the skin; Boyce and Surveyor (*Proc. Roy. Soc.*, March 9, 1893; *Brit. Med. Jour.*, September 22, 1894) in the muscles and elsewhere. Kanthack (*Jour. of Path. and Bact.*, 1892–93) describes the tissue changes which it produces in this situation as follows:—"In the earliest stages we have simply a reactive inflammation, the fungus being surrounded by round cells. Gradually the latter are replaced by typical granulation tissue, epithelioid cells, and vessels which appear in large numbers. At this time the various degeneration forms of the fungus"—the clubbing of the rays, pigmentation of mycelium, vitreous changes, loss of tinctorial qualities, and so forth—"are observed, and a pigment, varying in colour from yellow to dark brown, is observed in the tissues around the fungus. Gradually the granulation

cells give rise to fibrous tissue and we may then see the typical microscopical cysts or abscesses composed of the following structures passing from without inwards: (*a*) A fibrous ring (pigmented or not); (*b*) granulation cells; (*c*) pus cells or leucocytes, perhaps invading the fungus; (*d*) a finely granular detritus immediately around the organism; (*e*) the fungus itself. The latter may be at any stage of degeneration." The exact process by which the cysts and sinuses are formed has not been fully worked out; presumably, it is an extension of the process described by Kanthack, the lining membrane of the cysts and sinuses being the outcome of an inflammation which is excited in the tissues by the fungus, and which is evidence of an effort on the part of the body to protect itself by shutting off and extruding the invading parasite.

This fungus, so closely allied to actinomyces, has been successfully cultivated by Boyce and Surveyor, and also by Vincent; but hitherto, all attempts to grow it in the lower animals have failed. Unlike actinomyces, it will not grow readily in animal substances but flourishes in vegetable infusions or in media containing a proportion of vegetable matter. It differs also from actinomyces in certain minute morphological and tinctorial qualities; so that though closely allied to the better-known fungus, apparently it is not specifically identical with it. Vincent has named it nocardia or streptothrix maduræ.

Black variety.—Although all observers are practically agreed in recognising the presence of a ray fungus in the white or ochroid form of mycetoma, there is not the same unanimity in regard to the presence and characters of fungus elements in the black or melanoid variety.

The individual black grains, floating in the discharge or lying in the tissues, in this form of mycetoma, vary in size from microscopic grains to masses of considerable bulk, as already mentioned. The surfaces of the smaller grains are distinctly mammillated, and the bodies themselves are firm and friable. Their

colour is not discharged by alcohol or chloroform, and is but slightly affected by caustic potash; but it is discharged by first boiling in caustic potash and subsequently transferring to distilled water. Certain of the grains—presumably the oldest—reveal no fungus under the microscope: but others, as Kanthack and Boyce have pointed out, show a distinct network of interlacing, broad, varicose, moniliform tubes with a manifest radiated arrangement. At the periphery these tubes may end in minute clubs. The walls of the tubes, as well as the intermediate substance, are pigmented. Such bodies do not specially suggest a ray fungus; but Kanthack, in one specimen of melanoid Madura foot, found examples in which a central interwoven mycelium was surrounded by a zone of characteristically clubbed rays. In this specimen the filaments were broad, often interrupted, not uniform in diameter, and presented small varicosities. Transition forms, connecting the more or less perfect type with the structureless black masses, could be traced. From this circumstance Kanthack concludes that the black masses are really the product or remains of the fungus described. The black pigment is never found free in the softened tissues, but is always closely surrounded by a dense, fibrous tissue, or it lies in cysts or sinuses.

The relationship of the white to the black variety.—The question suggests itself, are the two forms of Madura foot, the ochroid and the melanoid, caused by the same parasite, by varieties of the same parasite, or by a distinct species? In favour of the specific identity of the forms are the facts that black and white masses have been found together in the same case (Lewis and Cunningham and Boccaro); that they are co-endemic, that, with the sole exception of the colour, the clinical features and progress of the disease are identical in both forms; that pigment is often found in the tissues in the white variety; that the fungus of the latter often undergoes distinct pigmentary degeneration such as is often seen in human and

bovine actinomycosis. Against their identity are the rarity of their concurrence in the same individual; the large size of the mycelial filaments in the melanoid form; and the fact that the latter, unlike the white fungus, has hitherto resisted all attempts at cultivation.

The pathological significance of the fungus.—Most pathologists agree in regarding the ray fungus as the cause of the disease in, at least, the white variety of mycetoma. Cunningham, however, has demurred (*Sc. Mem. by the Med. Off. with the Army in India*, No. 9, 1895) to this conclusion, on the following grounds:—"1st, that a certain number of cases occur in which, whilst all the essential symptoms of the disease are present, there is an entire absence of any concretions of either the black or white variety and of the fungal elements ordinarily associated with them; 2nd, that the fungal elements which ordinarily occur in connection with the two varieties of the disease are of absolutely unlike character, those associated with the white variety resembling those of actinomyces, and those of the black variety forming sclerotiæ like those of the sclerotiniæ and other allied ascomycetes; 3rd, that the very formation of sclerotioid bodies is a process which is normally indicative of a cessation of vegetative growth dependent on exhaustion of nutritive supply, and therefore one which could not occur were the normal tissues the proper site for the development of the parasitic elements." Cunningham suggests that the fungus vegetates on a soil previously prepared for it by the true, and as yet undiscovered, cause of the disease; and hints that possibly the endarteritis already referred to may be the primary effect of the true germ, and the cause of the softening of the tissues, which thus become a suitable nidus for the actinomyces-like fungus that subsequently enters accidentally from without. According to this view, the ray fungus is not a necessary element in the pathological process but merely an accidental epiphenomenon.

Until irrefutable evidence, such as can only be

supplied by the successful inoculation of cultures of the ray fungus taken from both the white and the black varieties, is obtained, similar objections can always be raised to accepting these parasites as the true cause of mycetoma. Nevertheless, the intimacy and frequency of their association with this disease are so marked that the provisional assumption of such a relationship seems to be justifiable.

Mode of entrance of the fungus. Nothing is known on this point. It is conjectured that the fungus may be a usual parasite on some plant, and that it finds an entrance into the tissues of man through a wound in the skin. The facts of its occurring almost invariably on the feet or hands, and principally in bare-footed agriculturists, favour this view. No distinct relationship has been traced between the disease and any particular type of soil or vegetation.

Treatment.—The only effective treatment, in the case of implication of a considerable part of the foot or hand, is amputation. This must be performed well above the seat of the disease; for it must be borne in mind that the long bones may be implicated as well as the small bones, and that unless the entire disease be removed it will recur in the stump. Complete removal is not followed by relapse. If a toe, or a small portion of the foot or hand, is alone involved, this may be excised with success. Iodide of potassium, which seems to be so potent a remedy in actinomycosis, has been tried in madura foot but without success.

DHOBIE ITCH.

In view of the recent researches of Sabouraud and others on the ringworms of Europe, there can be little doubt that the ringworms of warm countries are attributable to a large variety of fungus forms, probably many of them derived from the lower animals. Although, in a general way, we are familiar enough with the clinical features of these ringworms, their specific germs have not as yet been very closely studied. By the

lay public all epiphytic skin diseases, more especially all forms of intertrigo, are spoken of as dhobie (washerman's) itch, in the belief, probably not very well founded, that they are contracted from clothes which have been contaminated by the washerman. There are many sources of ringworm infection in warm climates besides the much maligned dhobie.

In the tropics, native children often exhibit dry, scurfy patches of ringworm on the scalp; and the skin of the trunk and limbs of adults is not infrequently affected with red, slightly raised, itching rings, or segments of rings, of trichophyton infection. Sometimes these rings enclose areas many inches in diameter.

Pityriasis versicolor is also very common in the tropics. It is the usual cause of the pale, fawn coloured, scurfy patches so frequent a feature on the dark skinned bodies of natives. On the dark, pigmented skin of negroes, Indians, and dark-complexioned Chinese, the patch of pityriasis—contrary to what obtains in Europeans and light-skinned Chinese—is paler than the healthy integument surrounding it. The pigment in the fungus (microsporon furfur) and the profuse growth of the latter conceal, as a coat of yellow paint might do, the dark underlying natural pigment of the skin.

The expression *dhobie itch*, although applied to any itching, ringworm like affection of any part of the skin, most commonly refers to some form of epiphytic disease of the crutch or axilla. There are at least three species of vegetable or bacterial parasites which in the tropics are prone to attack these situations -namely, the trichophytons or ordinary body ringworms, the microsporon minutissimum of erythrasma, and the germ of the disease I have described under the name pemphigus contagiosus.

The suffering which some of the forms of dhobie itch gives rise to is often very great. In hot, damp weather especially, the various germs proliferate very actively, producing what is often a severe dermatitis.

The [illegible] is scratching and [illegible] from [illegible]. It [illegible] The [illegible] is [illegible] The [illegible] and [illegible] [illegible] [illegible]

FIG. 81.—TINEA IMBRICATA.

To face p. 581.

microsporon—furfur and minutissimum—dhobie itch are more easily cured than the trichophyton varieties.

Treatment.—After a thorough use of soap and water, the application of Vleminck's solution of sulphuret of calcium (1 oz. quicklime, 2 oz. precipitated sulphur, 15 oz. water, boiled together in an earthenware vessel till reduced to 10 oz.; decant the clear sherry-coloured fluid after subsidence) every night for three or four times, generally brings about a rapid cure. A tincture of the leaves of cassia alata painted on, or the crushed leaves themselves well rubbed in, are equally successful. If these fail, chrysophanic acid ointment, twenty grains to the ounce of vaseline, rubbed in twice a day till a slight erythema shows at the edge of the diseased patch, is almost invariably successful. When prescribing chrysophanic acid the physician must be careful to inform the patient of its staining effect on clothes; to warn him to stop its use so soon as the erythematous ring shows; and to be careful not to apply the ointment to the face. For the ringworms of the thick-skinned natives linimentum iodi freely applied, and of double strength, is the best remedy.

Prophylaxis.—The various forms of crutch dhobie itch may be avoided by wearing next the skin short cotton bathing drawers and changing them daily, at the same time powdering, after the daily bath, the axillæ and crutch with equal parts of boric acid, oxide of zinc, and starch.

TINEA IMBRICATA* (Fig. 81).

Definition.—A form of body ringworm peculiar to certain Eastern oceanic tropical climates, produced by a trichophyton, and characterised by a concentric arrangement of closely set rings of scaling epidermis.

Geographical distribution.—This peculiar form of trichophyton disease is strictly confined to warm climates. It is principally met with in the Eastern Archipelago and in the islands of the South Pacific,

* *Brit. Journ. of Dermatology*, No. 39, vol. iv.

although it has been found to extend westward as far as Burma, and northward as far as Foochow and Formosa on the coast of China. In many of the islands of the South Pacific it affects a large proportion of the inhabitants; in some islands quite one half. There is good reason to believe that its area of distribution is gradually extending. Thus Turner and Koniger tell us that it was formerly unknown in Samoa and Bowditch Islands, where it is now very prevalent. Dr. Daniels also informs me that it was introduced for the first time into Fiji by some Solomon Islanders in 1870; by 1872, he says, it had become general among the Fijians. We have no accounts of such a disease in Africa or America, it is probable, however, that ere long it will be introduced into the tropical parts of both of these continents. Once introduced, it spreads very rapidly in countries with a damp, equable climate and a temperature of between 80° and 90° Fahr. Very high or low temperatures and a dry atmosphere are inimical to its extension.

Symptoms. Tinea imbricata is easily recognised. At first it may be confined to one or two spots on the surface of the body; but usually, in a short time, it comes to occupy a very large area. It does not generally affect the soles and palms, although it may do so; nor is the scalp a favourite site. Dr. Oswald Baker remarks that it avoids the crutch, the axillæ, and the nails. With these exceptions it may, and commonly does, sweep over and keep its hold on nearly the entire surface of the body, so that after a year or two a large part of the skin is covered with the dry, tissue-paper like scales, arranged in systems of concentric parallel lines, absolutely characteristic of the disease.

An inoculation experiment readily explains the production of the scales, their concentric parallel arrangement, and the mode of extension of the patches. About ten days after the successful inoculation of a healthy skin with tinea imbricata, the

epidermis at the seat of inoculation is seen to be very slightly raised and to have a brownish tinge. Presently the centre of this brownish patch—perhaps a quarter of an inch in diameter—gives way and a ring of scaling epidermis, attached at the periphery but free, ragged, and slightly elevated towards the centre of the spot, is formed. In a few days this ring of epidermis has extended so as to include a larger area; and now a second brown spot appears at the site of the first brown spot and in the centre of the primary scaling, expanding ring. This second spot, in its turn, gives way, producing a second and similar scaling ring, which also expands, following the first ring in its extension. Later a third and fourth ring form in the same way; and so on, until the entire surface of the body is covered with one or more systems of concentric parallel scaling rings, which follow each other like the concentric ripples produced by a stone falling into a pond of water.

The scales, if not broken by rubbing, may attain considerable length and breadth; but, of course, their dimensions are very much influenced by the amount of friction they are subjected to. Usually they are largest between the shoulders—that is, where the patient has a difficulty in scratching himself. The lines of scales are from one-eighth of an inch to half an inch apart. The hair of the scalp is not injured.

The fungus.—On detaching a scale and placing it under the microscope, after moistening with liquor potassæ, a trichophyton-like fungus can be seen in enormous profusion. The parasite evidently lies between epidermis and rete, and by its abundance causes the former to peel up. As the fungus does not die out in the skin travelled over, it burrows under the young epithelium almost as soon as this is reproduced. Hence the peculiar concentric scaling and the persistency of the disease throughout the entire area involved. When the scales are washed off by the vigorous use of soft soap and hot water, the surface of the skin is seen to be covered with parallel lines of

a brownish colour—evidently the slightly pigmented fungus proliferating and advancing under the young epidermis.

Diagnosis.—From ordinary ringworm it is easily distinguished by the absence of marked inflammation or congestion of the rings, by the abundance of the fungus, by the large size of the scales, by the concentric arrangement of the many rings or systems of rings, by the non-implication of the hair, and, according to Dr. Oswald Baker, by the avoidance of crutch and axillæ. From ichthyosis it is distinguished by the concentric arrangement of the scaling, by the peripheral attachment of the scales, and by the presence of abundant fungus elements.

Treatment.—The best treatment for tinea imbricata in natives is the free application of strong linimentum iodi. Limited patches might be treated with chrysophanic acid ointment (twenty grains to one ounce) or by the inrubbing of bruised cassia alata leaves. Sulphur ointment or sulphur fumes act very slowly and unsatisfactorily. Clothes should be boiled or burned.

Prophylaxis.—Dr. Daniels informs me that tinea imbricata is comparatively rare in Tonga. This circumstance the natives attribute to their custom of oiling the body. Dr. Daniels remarks that since the Fijians adopted of late years the same practice, the disease has become somewhat less prevalent among them. Cleanliness, and the immediate and active treatment of any scaling spot, should be carefully practised in the endemic countries.

PINTA.

Definition.—An epiphytic disease characterised by peculiar pigmented patches on the skin.

Geographical distribution.—In certain districts in tropical America—especially along the river banks, in Mexico, Central America, Venezuela, Colombia, Bolivia, and one or two places in Peru, Chili, and Brazil—the district between the Juciparana and the Santo Antonio rivers (Magalhães, private letter)—

there occurs an epiphytic skin disease characterised by peculiar red, or blue, or black, or white piebald spotting of the skin on a part, or on the whole, of the body. The patient emits an offensive odour, sometimes compared to that of a mangy dog or of dirty linen. Desquamation and itching of the patches are also features of the disease. It entails no constitutional disturbance, and no danger to life. Like other epiphytic diseases, want of personal cleanliness has a great deal to do with the prevalence of pinta in the districts mentioned, for it is rare in cleanly whites or well-to-do negroes; the dirty Indians and the poor half-castes are those most frequently affected. In some districts it occurs in nearly a tenth part of the inhabitants. Lately a similar disease has been seen in North Africa.

Pinta commences at one or two points, the rest of the surface becoming infected in turn by extension or by auto-contagion. In the first instance, the hands or face, or some other exposed part is attacked. The original patch may be white, red, blue, or black. It gradually increases in size, becoming scurfy and itchy, particularly when the surface is warm. As the patches spread they assume a variety of shapes. Fresh spots appear in the neighbourhood of the parent spots, into which, in course of time, they tend to merge; so that ultimately large patches of discoloured skin are formed. The palms of the hands and the soles of the feet are not attacked. On the scalp becoming affected the hair turns white and thin and ultimately falls out. When fully developed, the disease produces a very grotesque appearance. It is probable that the white patches are not epiphytic, as they neither itch nor desquamate; very likely they are ordinary leucodermia, brought about by disturbance of the natural pigmentation of the skin by the parasite which had subsequently died out. Sensation and the glandular functions of the skin are not affected; although, in consequence of the scratching, the implicated parts may become cracked or ulcerated.

Two types of the disease have been named—the superficial epidermic and the deep epidermic; the former being represented by black and blue patches which spread rapidly; the latter including the red and white patches, apparently involving the rete and deeper layers of the epidermis, spreading more slowly, and, at the same time, being more difficult to cure. The various forms and colours may concur in the same individual; but a given patch, once established, does not change colour.

Pinta is contagious and attacks both sexes and any age. Unless properly treated, it may last for years.

Pathology.—If one of the scales is moistened with liquor potassæ and placed under the microscope, black spores and a white, highly refracting mycelium are found. The spores are round or oval, measuring 8 to 12 μ in diameter Abundant pigment is seen floating in a yellowish fluid in the interior of the spore. The mycelial filaments are short, non-branching, tapering from a broad base to a blunt point by which each filament is attached to a single spore, like the stalk to a cherry. The mycelium measures from 18 to 20 μ in length by 2 μ in breadth. The differences in the colour of the patches probably depend on differences in the pigmentation of the fungus.

Diagnosis. This disease is readily diagnosed from leprosy by the absence of anæsthesia in the patches, and by the colour of the spots; from erythrasma, from ringworm, and from pityriasis versicolor by the colour, and by the microscopical characters of the fungus.

Treatment.—Chrysophanic acid, preparations of sulphur, strong liniment of iodine, and other epiphyticides are indicated. Cleanliness and the destruction of old clothes are indispensable.

PIEDRA.

This peculiar epiphytic affection of the hair is very common in certain districts of Colombia, South America. So far as known, it is confined to the

inhabitants of that country, of whom a considerable proportion, both male and female, and apparently belonging to all the races represented there, are affected.

According to Juhel-Rénoy (*Ann. de Derm. et Syph.*, Dec. 25th, 1888), whose observations practically coincide with the earlier accounts by Desenne, Cheadle, Morris and others, the hairs of the affected scalp are dotted over at irregular intervals with numerous twenty three in a hair sixty centimetres in length minute, gritty nodosities. These are barely visible to the naked eye, but distinctly perceptible to the touch when the hair is drawn between finger and thumb. The affected hairs are bent and twisted, and tend to produce matting and knotting. The little nodosities, which, though very firm, are not so hard as the name piedra—a stone—would indicate, being easily cut through with a sharp knife or scissors, are paler than the hair they surround or partly surround like a sheath. When a comb is drawn through the hair a sort of crepitation is produced, doubtless by the friction against the hard particles.

Under the microscope these excrescences are found to consist of a number of spore-like bodies, easily made apparent by soaking the hair in liquor potassæ after washing in ether. The spores (which are twice the size of trichophyton spores and remarkably refringent) from mutual pressure are polyhedral, and together form a sort of tessellated mosaic, the elements of which seem to be held together by a greenish soluble cement in which a number of minute bacteria like rods are incorporated. The shaft of the hair is not eroded nor affected in any way; it can be seen intact through the encrusting fungus.

Piedra is supposed by some to be induced by the mucilaginous hair applications in vogue among the Colombians. Although Juhel-Rénoy has given to it the name "trichomycose nodulaire," it must not be confounded with the trichomycosis nodosa of Paterson (the leptothrix of Wilson), which is quite a different

affection and common enough on the axillary, scrotal, and face hair in Europe and elsewhere Neither must it be confounded with trichorexis nodosa, a non-parasitic disease of the hair-shaft, which is split up at different points into brush-like bundles of fibres and is thus easily fractured ; nor with moniliform hair (monilethrix, Crocker), a congenital, hereditary, and also non-parasitic disease.

Treatment.—Cleanliness, the free use of soap, and the application of some epiphyticide should suffice for cure. Should such means fail, doubtless shaving the scalp would be effectual.

IV. *Caused by animals.*

THE CHIGGER OR SAND FLEA (*Pulex penetrans*).

This insect, formerly confined to the tropical parts of America (30° N. to 30° S) and to the West Indies, appeared on the West Coast of Africa for the first time about the year 1872. Since that date, not only has it spread all over the tropical parts of that continent but, according to Blandford (*Entomologists' Monthly Mag.*, May, 1894), has made its appearance in China As a cause of suffering, invaliding, and indirectly of death, it is an insect of some importance.

Fig 82. Chigger (*pulex penetrans*). (*Blanchard*)

The chigger (Fig. 82) is not unlike the common flea (*pulex irritans*) both in appearance and, with one exception, in habit. It is somewhat smaller in size, the head being proportionately larger and the abdomen deeper than in the latter insect. In colour it is red or reddish brown. Like the flea, its favourite haunt is in dry, sandy soil, the dust and ashes in badly kept

native huts, the stables of cattle, poultry pens, and the like. It greedily attacks all warm-blooded animals, including birds and man. Until impregnated, the female, as well as the male, is free, feeding intermittently as opportunity offers; but so soon as she becomes impregnated she avails herself of the first animal she encounters to burrow diagonally into its skin where, being well nourished by the blood of the host, she proceeds to ovulation. By the end of this process her abdomen, in consequence of the growth of the eggs it contains, has attained the size of a small pea. (Fig. 83.) The first anterior and the two posterior segments do not participate in the enlargement, the latter acting as a plug to the little hole made by the animal on entering the skin. When the ova are mature they are expelled and fall on the ground. In a short time a thirteen-ringed larva is hatched out from each egg. This larva presently encloses itself in a cocoon from which, in eight to ten days, the perfect insect emerges.

Fig. 83.—Chigger: impregnated female. (*Blanchard.*)

During her gestation the chigger causes a considerable amount of irritation. In consequence of this, pus forms around the distended abdomen, which now raises the inflamed integument into a pea-like elevation. After the eggs are laid (according to some, before this process) the superjacent skin ulcerates and the chigger is expelled, leaving a small sore which, if infected by any pathogenic micro-organism, as the bacterium of phagedæna or of tetanus, may lead to grave consequences.

Naturally, being nearest the ground, the feet are the parts most commonly infested by chiggers. The soles of the feet, the skin between the toes, and that at the roots of the nails are favourite situations. Other parts of the body are by no means exempt; the

scrotum, penis, the skin around the anus, the thighs, and even the hands and face are often attacked. Usually only one or two chiggers are found at a time; occasionally they are present in hundreds, the little pits left after their extraction being sometimes so closely set that parts of the surface may look like a honeycomb.

Treatment.—In chigger countries, houses, particularly the ground floors, must be frequently swept and accumulation of dust and débris prevented. The housing of cattle and poultry must be similarly attended to. The floors should be sprinkled frequently with carbolic water, insect powder, or similar insecticide. Walking barefooted must be avoided. Bathing must be practised daily, and any chiggers that may have fastened themselves on the skin at once removed. They may be killed by pricking them with a needle, or by the application of chloroform, turpentine, mercurial ointment, or similar means, after which they are expelled by ulceration. The best treatment, however, is not to wait for ulceration but to enlarge the orifice of entrance with a sharp, clean needle and neatly to enucleate the insect entire. Some native women, from long practice, are experts at this little operation. The part must be carefully dressed and protected until whole.

MYIASIS.

THE SCREWWORM (*Lucilia macellaria*).

This is the larva of a dipterous insect (Fig 84) common in certain parts of America, from the United States to the Argentine. The insect lays her eggs on the surface of wounds, and in the ears and nasal fossæ of persons sleeping in the open air. From these eggs the larvæ are hatched. These are white, about three-quarters of an inch in length, and formed of twelve segments carrying circles of minute spines so arranged as to give the creature a screw like appearance, hence the vulgar name. They burrow in the tissues, devouring the mucous membranes, muscles, cartilages,

periosteum, and even the bones, thereby causing terrible sores and, not infrequently, particularly when they attack the ear or nasal fossæ, by penetrating to the brain, death. In thirteen cases collected by

Fig 84. Screwworm (*Blanchard.*)

Laboulbène nine proved fatal; in thirty-one collected by Maillard twenty-one died.

If treated properly and in time, by injections of chloroform, carbolic acid, turpentine, and similar substances, the patient may be saved; neglected, he will most probably die. If necessary, the frontal sinuses, the antrum, and other bony cavities must be opened to secure the expulsion of the larvæ. In countries where this pest occurs, bloody and offensive discharges from the nostrils should be carefully investigated and, if found to be caused by the screwworm, vigorously treated.

VER MACAQUE (*Dermatobia noxialis*) (Fig. 85).

This is the larva of an American fly the identity of which, until observations by Blanchard (*Bul. de*

Fig. 85. Dermatobia noxialis. (*Blanchard.*)

la Soc. Cent. de Med. Vétérinaire, July 9th, 1896), was somewhat doubtful, some naturalists considering

that it might be the larva of *D. cyaniventris*. Blanchard has now shown that the latter never attacks man or domestic animals. The larva is somewhat larger than the preceding but, though larger, is much less formidable. The fly occurs about wooded lands and deposits her eggs on cattle and dogs, and occasionally on man. When hatched out, the larvæ penetrate the skin and produce an inflamed swelling about the aperture of entrance, from which a sero-purulent fluid, containing the black fæces of the larva, exudes. Depied (*Arch. de Méd. Nav.*, February, 1897) says that he has twice encountered this larva (the identity of which he ascertained by developing the insect) in the scalp of Tonquinese.

VER DU CAYOR (*Ochromyia anthropophaga*).

This insect and larva occur in the district of Cayor, Senegambia. The larva burrows into the skin and produces a small inflamed swelling, from which it emerges in from six to seven days.

In Africa, and in many other parts of the tropical world, similar anthropophagous larvæ, which, however, have not yet been identified, are frequently encountered.

LEECHES.

In the grass and jungle lands of many tropical and subtropical countries land leeches, probably of several species, often occur in great abundance; so much so that in some circumstances they may prove to be something more than a nuisance. The *Hæmadipsa Ceylonica* is one of the most active, as well as best known, of these. Before feeding it is about an inch in length and about the thickness of a knitting-needle. It clings to a leaf or twig awaiting the passing of some animal, on whom it springs with remarkable activity; it at once attaches itself to the skin, and proceeds to make a meal on the blood. Animals are sometimes killed in this way; men even have been known to succumb to the repeated small bleedings by these pests. It is necessary, therefore,

when passing through jungle lands in which leeches abound, to have the feet and legs carefully protected. The bite is not infrequently the starting-point for a troublesome sore.

In the south of Europe and in the north of Africa the horse leech, *Hæmopis sanguisuga*, sometimes gets into the gullet and nostrils of men as well as of animals. It has occasionally caused death by entering and occluding the air-passages. In Formosa I heard of and saw several instances of a similar form of parasitism, both in men and monkeys. To what particular species the leech in these cases belonged I do not know. Doubtless when very young they were taken in unperceived with foul drinking water and, wandering around the soft palate, found their way into the nose. Occasionally, in the cases I refer to, the animal would protrude from the nares and wander over the upper lip. For a long time they contrived to elude all attempts at capture. By dipping the face in cold water they could generally be persuaded to show themselves. In one instance the leech dropped out spontaneously. In another—an American naturalist who had been travelling much in the interior of Formosa, and who had suffered from severe headache and profound anæmia, the result of repeated epistaxis—I succeeded in removing the leech by attaching through a speculum a spring forceps to its hinder end, and afterwards injecting salt and water. It would be well, therefore, to bear in mind that persistent headache, associated with recurring epistaxis, in tropical countries, may be caused by a leech in the nostril.

SECTION VII. LOCAL DISEASES OF UNCERTAIN NATURE.

CHAPTER XXXVIII.

GOUNDOU AND AINHUM.

GOUNDOU OR ANAKHRE (*Gros Nez*) (Fig 86).

On December 10th, 1882, Professor A. MacAlister read a paper before the Royal Irish Academy on what were termed the horned men of Africa. In the *British Medical Journal* of December 10th, 1887,

Fig. 86.—Goundou or anakhre (*Maclaud*)

Surgeon-Major J. J. Lamprey gave further details, illustrated with drawings, on the same subject. He had seen three such cases on the West Coast of Africa, all of them Fantees; one came from the Wassan territory, one from the Gamin territory, the third was a visitor to Cape Coast Castle.

In the *Archives de Médecine Navale*, January, 1895, Dr. Maclaud, of the French Marine, calls attention to what is manifestly the same affection, which, according to him, occurs in a considerable proportion—one or two per hundred—of the inhabitants of certain villages on the Ivory Coast. The natives call it *goundou* and also *anakhre*. Maclaud says it is confined to the riveraine districts of the lower Camoe; according to the information he received, if found elsewhere it is only in the person of individuals who at some time or other had previously resided in this district. Lamprey's observations, however, prove that this peculiar affection has a considerably wider distribution.

According to Maclaud, the disease usually commences soon after childhood, although adults may also be attacked. The earliest symptoms are severe and more or less persistent headache, which, after a time, is associated with a sanguino-purulent discharge from the nostrils, and the formation of symmetrical swellings the size of a small bean at the side of the nose. Apparently the swelling affects the nasal process of the superior maxilla. The cartilages are not involved; and, although Maclaud does not refer to this point, it may be assumed that the nasal ducts are also not involved. After continuing for six or eight months, the headache and discharge subside. Not so the swellings, which persist and continue slowly and steadily to increase until, in time, they may attain the size of an orange, or even of an ostrich's egg. As they grow the tumours, encroaching on the eyes, interfere with the line of vision and finally destroy these organs. There is no pain in the tumours themselves; they appear to consist of a thin shell of bone, and, judging from the percussion note, are hollow. The superjacent skin is not involved, being healthy-looking and freely movable. The tumours are oval, with the long axes directed downwards and slightly from within outwards. Lamprey's drawings give a more elongated form and horizontal

direction. They look, according to Maclaud, when of moderate dimensions, something like two half-eggs

Fig. [illegible] a West Indian child. (*Dr. Lewis Strachan.*)

laid alongside the nose, one on each side. The nostrils are bulged inwards, and more or less obstructed; but, in the later stages at all events, there is no discharge,

neither can any breach of the mucous surface be detected. The hard palate is not affected in any way.

Dr. Maclaud had no opportunity of ascertaining by *post-mortem* examination or by surgical operation the nature of this singular disease. He inclines to the opinion that, in the first instance, the process is started by the larvæ of some insect which find their way into the nostrils. I would point out, however, that the symmetry of the growths is difficult to account for on this hypothesis. Dr. Maclaud observed on one occasion a similar affection in a chimpanzee.

Dr. Henry Strachan (*Brit. Med. Jour.*, Jan. 27, 1894) records and illustrates (Fig. 87) an instance of what may be the same affection in a West Indian negro child. In this instance the swellings were congenital, and had only increased in proportion to the child's growth. They were hard, smooth, bony masses, somewhat of the shape and size of an elongated pigeon's egg, and sprang from the nasal process of the superior maxillary and nasal bones. For æsthetic reasons they were removed by the chisel, and were found to consist of compact bone externally with a cancellous core. Dr. Strachan states that he had seen two similar cases, and had often noted a "ridge" in this part of the face of West Indian negroes. He suggests that this feature in West Indian negroes may be an example of atavism, referable to some tribal peculiarity of the original West African stock.

AINHUM (Fig. 88).

This is a disease of a very peculiar character, affecting the toes, particularly the little toes, of negroes, East Indians, and other dark-skinned races.

It commences as a narrow groove in the skin, almost invariably on the inner and plantar side of the root of the little toe. It may occur on one foot only, or in both feet simultaneously, or it may affect one foot after the other. The groove, once started, deepens and extends gradually round the whole circumference

of the toe. As the groove deepens—it may be, though not necessarily, with some amount of ulceration -the distal portion of the member is apt to swell to a considerable size, as if constricted by a ligature. There is little or no pain, although there

Fig. 88. Ainhum.

may be inconvenience from the liability to injury to which the dangling and now everted toe is exposed. In the course of years the groove slowly deepens and finally the toe drops off or is amputated. The groove may either correspond with a joint, or it may be formed over the continuity of a phalanx. In rare instances, after the two distal phalanges have dropped off or been amputated, the disease recurs in the stump and the proximal phalanx is in its turn thrown off. Of the other toes the fourth is the one which is most frequently affected, very rarely are the third, or

second, or great toes attacked. In the Army Medical Museum at Washington, U.S.A., there is a wax model representing a case of this or a similar affection in which all the toes had been thrown off and the disease was making progress in the leg. Ainhum is very rare in women or children, being most common in adult males. It runs its course in from one to ten or even more years.

On section it is found, as a rule, though not invariably, that the panniculus adiposus of the affected toe is much hypertrophied, that the bone is infiltrated with fatty matter, and that the other tissues are correspondingly degenerated. Sometimes the bone is thinned, or even altogether absorbed. At the seat of constriction a line of hypertrophy of the epithelial layers, and of atrophy of the papillary layer of the skin, together with a band of fibrous tissue, more or less intimately connected with the derma, surround, in whole or in part, the narrow pedicle.

Nothing is known as to the true nature and cause of this disease, to which the European and white-skinned races are not, but to which the African races, particularly the negroes of the West Coast, are specially liable. Some have suggested that it is a trophic lesion depending upon some nervous affection; and the occurrence of severe loin pains, which Dupouy says he remarked at the commencement in some of his cases, as well as the tendency of the affection to run in families, as noted by Da Silva Lima, affords a certain amount of support to this view. Others suggest that it is a manifestation of leprosy; others that it is a form of sclerodermia; others, again, and on equally inadequate grounds, that it is produced artificially by intentional ligature or by the wearing of toe rings. My own impression is that it is provoked, at all events in the first instance, by wounds so easily inflicted on bare feet in walking through grass or jungle. The fold of skin in which the lesion of ainhum commences is very liable, especially in the splayed out toes of the negro, to be wounded in this way. If we examine the

under surface of the joint flexures of the toes in many individuals of this race, even of those not affected with ainhum, we often find the skin, particularly at the proximal joint of the little toe, thick, rough, scaling, and sometimes even ulcerated. One can understand that continued irritation of this sort, produced and kept up by wounds from sharp grasses and so forth, would in time give rise, especially in the dark-skinned races so prone to keloid, to fibrotic changes in the derma, which might very well end in a sort of linear cicatricial contraction and, ultimately, in slow atrophying strangulation of the affected member. The disease is said, however, to have been seen in those who wear shoes; but unless it could be shown that such individuals had always worn shoes, this objection to the explanation offered would not apply. I have seen a case in which the entire integument of the little toe was involved in a sclerodermia, and the part in consequence shrunken and hide-bound, whilst the little toe of the other foot was affected with well-marked ordinary ainhum; the process was diffuse, as it were, on the one side and localised on the other.

Treatment.—It has been suggested that division of the constricting fibrous band would delay the evolution of the disease. In the early stage this might be tried. When troublesome, the affected toes should be amputated.

THE END.

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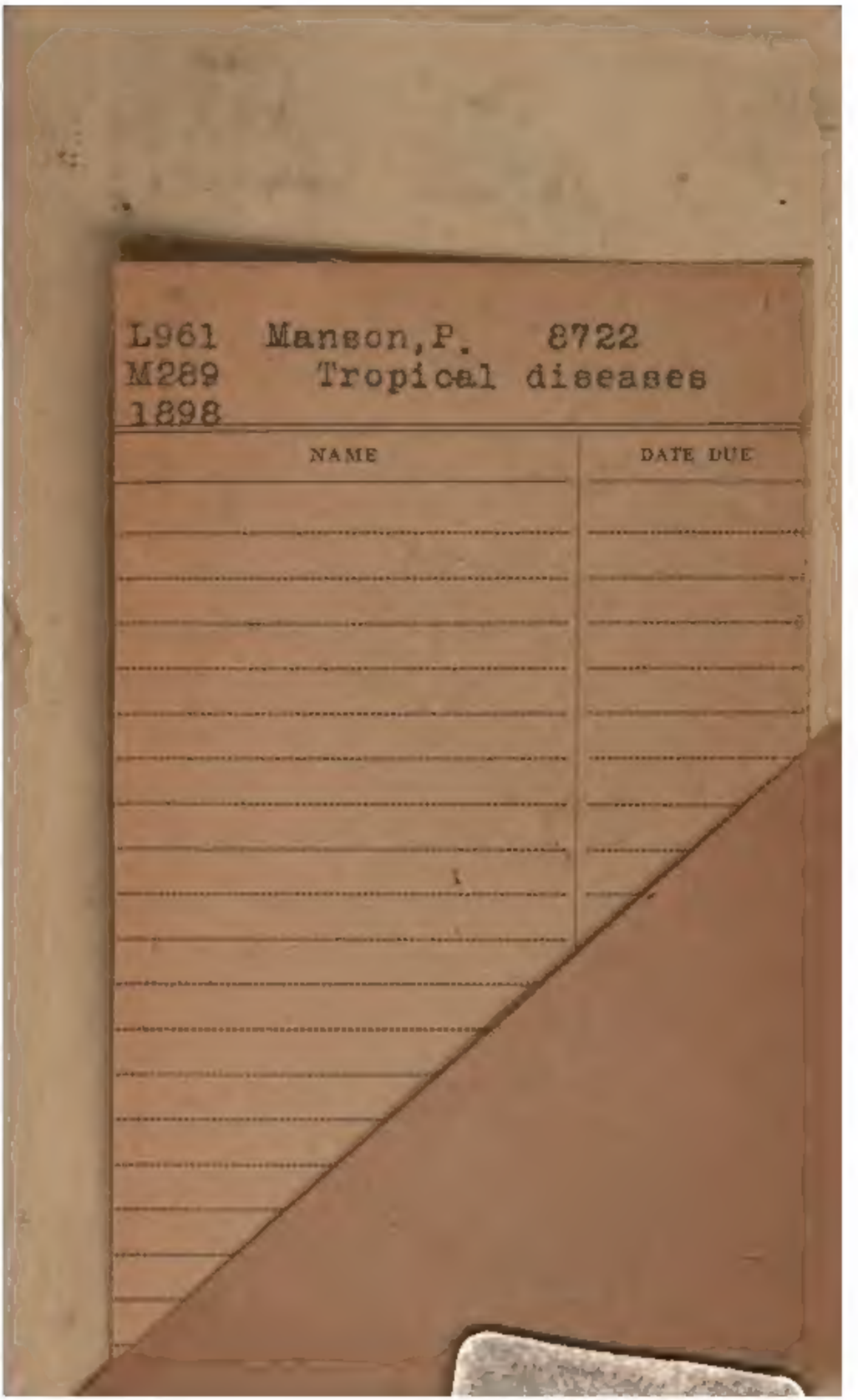
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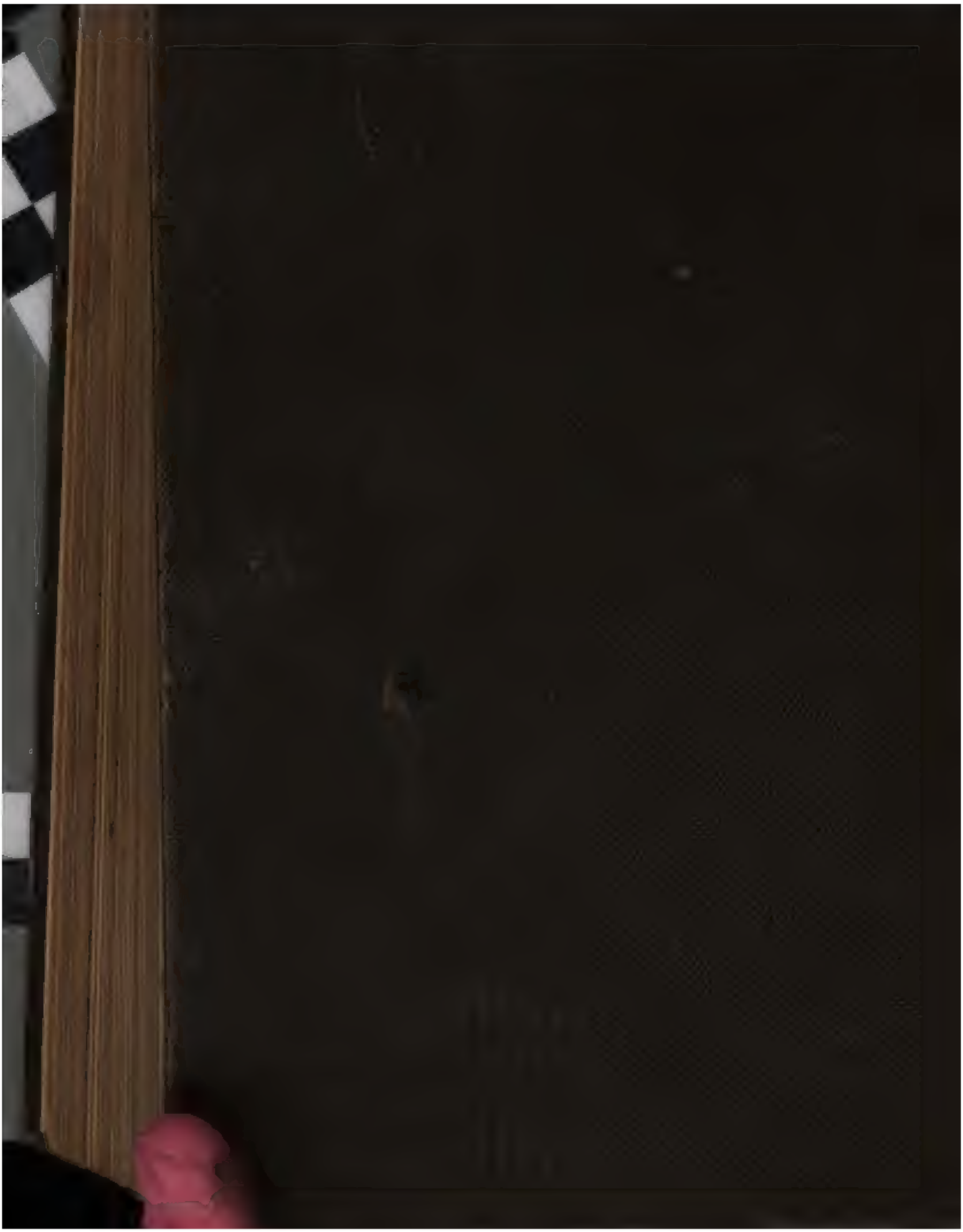
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